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LIVER BLOOD FLOW, HEPATIC GLUCOSE PRODUCTION, AND SPLANCHNIC OXYGEN CONSUMPTION IN NORMAL DOGS AND FOLLOWING ECK FISTULA. LIVER BLOOD FLOW BEFORE AND AFTER SPLENECTOMY

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THE purpose of this study has been to estimate the liver blood flow, hepatic glucose production, and splanchnic oxygen consumption in normal dogs and following Eck fistula. In addition, liver blood flow determinations were carried out on dogs before and after splenectomy. Employing the bromsulphalein method there was a 50 per cent reduction of blood flow following Eck fistulas, glucose production was unaltered, and splanchnic oxygen consumption was reduced approximately one half, indicating that in the fasting state the liver is responsible for one half of the total splanchnic oxygen consumption. The effect of splenectomy on liver blood flow was unpredictable under these experimental conditions.

Previous estimations of liver blood flow have been carried out by a number of investigators employing a variety of techniques, and their results are in general agreement. Burton-Opitz (8, 9, 10), Barcroft and Shore, and Grab, Janssen, and Rein were early workers in this field. Blalock and Mason determined liver blood flow by direct measurement and found that canine blood flow per gram of liver tissue per minute varied from 0.46 to 1.12 milliliters, the average being 0.82 milliliter. Grindley, Herrick, and Mann measured liver blood flow in dogs by the thermostromuhr method of Baldes and Herrick, and their results are similar to those reported by Blalock. Lipscomb and Crandall reported slightly higher blood flow values employing a urea output method.

The development of the bromsulphalein clearance method (5, 6) has facilitated recent studies of liver blood flow and liver metabolism. This method has been used exclusively in these experiments.

METHODS

Estimations of hepatic blood flow were carried out in accordance with the bromsulphalein clearance principle of Bradley. All animals were studied in the postabsorptive state. Diets were unrestricted prior to the evening preceding the tests, after which all food was withdrawn. The experiments were carried out under sodium pentobarbital anesthesia (approximately 40 mgm. per kgm. animal weight). All flows were calculated on the basis of at

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TABLE I.—ESTIMATED HEPATIC BLOOD FLOW, HEPATIC GLUCOSE PRODUCTION, AND SPLANCHNIC OXYGEN CONSUMPTION IN NORMAL DOGS

Dog	Weight kgm.	Liver weight gm.	EHBF ml./min.	Hepatic glucose output mgm./min.	Splanchnic oxygen consumption ml./min.
50–165*	12.7	434	540	60.5	35.6
44–29	16.8		1026	94.7	28.4
50–174	19.9	624	1025	34.5	24.0
50–166*	14.0		1304	44.0	26.4
50–159*	12.5		614	38.1	19.3
50–195*	19.3		597	39.6	33.3
50–164*	10.0	370	713	17.8	34.2
50–141*	11.3	500	1010		
49–188	15.9		735		
49–149**	13.2		672		
51–58**	12.9	320	749	31.4	15.8
51–29**	15.4	285	922	43.9	10.5
51–36**	12.5	204	564	25.3	26.7
51–24**	10.0	250	403	30.5	24.3

* Splenectomy performed later.
** Eck fistula performed later.

least four peripheral venous (P) and hepatic venous (H) bromsulphalein differences. Preliminary experiments had revealed no significant difference in the bromsulphalein concentrations in the inferior vena cava and the portal vein. Inasmuch as these values were found to be equal, the femoral vein was used as a source for peripheral bromsulphalein samples. Hepatic catheterization was accomplished fluoroscopically usually without incident. Upon occasion, this was unsuccessful due to insertion of the catheter in the azygos or diaphragmatic vein, with fluoroscopic simulation of a successful hepatic vein catheterization. Data obtained on these experiments were discarded. Following a priming dose of bromsulphalein, a constant intravenous infusion of bromsulphalein was started in concentrations of 350 milligrams per 100 milliliters of sterile normal saline. A 20 minute period was allowed for stabilization, during which a relatively constant peripheral blood level of bromsulphalein was attained. Following this, blood samples for bromsulphalein concentration, glucose, and oxygen content were collected at 10 minute intervals from the femoral and hepatic veins. An arterial blood sample was collected at the close of the experiment.

Blood glucose levels were determined by the method of Benedict. Care was exercised that the fresh samples were precipitated promptly in order to avoid glycolysis. Blood oxygen contents were determined by the manometric method of Van Slyke. Bromsulphalein concentrations were determined promptly, utilizing the Klett photoelectric colorimeter.

The control animals were divided into two groups: in one, Eck fistulas, and in the other, splenectomies were performed at a later date. Operations were performed under sodium pentobarbital anesthesia. In those animals in which Eck fistulas were done, a right subcostal approach was employed and the anastomosis performed over Eck clamps. Following this, the portal vein was ligated proximal to the entrance of the splenic vein. An adequate anastomosis was believed to have been constructed in each animal. No thrombosis occurred. In those animals undergoing splenectomy, a left rectus incision was used. Operations and postoperative course were not remarkable.

RESULTS

Estimation of liver blood flow. Data from a series of normal dogs are shown in Table I. This table represents a tabular summary of a series of similar experiments. A detailed account of one such experiment appears in Table II. No attempt is made to correlate the volume of flow with liver weight, animal weight, or surface area. The unitage of liver weight was discarded for two reasons: first, it is not known in all instances, and secondly, marked liver atrophy followed in Eck fistula animals, and this relays inaccurate flow-weight relationships. Although variations from 403 to 1,304 milliliters in liver blood flow per minute are to be noted in the normal control group, variations greater than 200 milliliters per minute in individual experiments were unusual. The average figure for the control normal animals is higher than those reported in which other methods of flow determination were employed.

TABLE II.—DETAILED DATA ON NORMAL DOG*

Period	Peripheral BSP mgm.% (P)	Hepatic BSP mgm.% (H)	P-H	Quantity BSP infused mgm./min.	Time min.	EHBF ml./min.	EHBF ml./min.
1.	3.14	2.31	0.83	2.06	20	248	428
2.	3.57	3.01	0.56	1.72	10	307	531
3.	3.41	2.76	0.65	1.79	10	275	475
4.	3.72	2.89	0.83	1.82	10	219	378

Period	Hepatic venous CO_2 vol. %	Hepatic O_2 vol.%	O_2 sat. vol. %	O_2 difference vol. %	EHBF ml./min.	Splanchnic O_2 consumption ml./min.
1.	49.86	13.04	68.1	5.36	428	22.97
2.	52.29	12.95	67.6	5.45	531	28.95
3.	49.09	13.09	68.3	5.31	475	25.2
4.	48.68	13.04	68.1	5.36	378	20.12
Arterial	40.78	18.40	96.1	Capacity 19.14 vol. per cent		

Period	Hepatic glucose mgm. % (H)	Peripheral glucose, mgm. % (P)	H-P	EHBF ml./min.	Hepatic glucose output, mgm./min.
1.	80	66	14	428	60
2.	83	77	5	531	26.1
3.	80	78	2	475	9.5
4.	91	84	7	378	26.5

*Dog 51-24, weight 10.0 gm., hematocrit 42 per cent.

TABLE III.—DETAILED DATA ON DOG* FOLLOWING ECK FISTULA

Period	Peripheral BSP mgm.% (P)	Hepatic BSP mgm.% (H)	P-H	Quantity BSP infused mgm./min.	Time min.	EHBF. ml./min.	EHBF. ml./min.
1.	3.78	2.91	.87	1.61	20	185	281
2.	3.98	2.79	1.19	1.85	10	155.5	236
3.	4.28	2.85	1.43	2.13	10	149	226
4.	4.59	2.94	1.65	1.78	10	108	193

Period	Hepatic venous CO_2 vol. %	Hepatic O_2 vol.%	O_2 sat. vol. %	O_2 difference vol. %	EHBF ml./min.	Splanchnic O_2 consumption ml./min.
1.	48.09	13.95	68.3	5.61	281	15.77
2.	45.32	13.76	67.4	5.80	236	13.7
3.	46.19	13.86	67.9	5.70	226	12.82
4.	48.09	13.71	67.1	5.85	193	11.3
Arterial	43.72	19.56	95.8	Capacity 20.41 vol. per cent		

Period	Hepatic glucose mgm. % (H)	Peripheral glucose mgm. % (P)	H-P	EHBF ml./min.	Hepatic glucose output mgm./min.
1.	91	81	10	281	28.1
2.	88	81	7	236	16.5
3.	90	80	10	226	22.6
4.	98	80	18	193	34.8

*Dog 51-24, weight 10.0 kgm., hematocrit 34 per cent.

Results following Eck fistula.—In all animals following Eck fistulas marked reductions in estimated liver blood flow (EHBF) were recorded, approximating 50 per cent of the control flow. This is demonstrated in Tables II, III, and IV. Table II represents data obtained upon a normal dog upon which an Eck fistula was performed later. In Table III the postoperative data appear. Table IV shows a series of similar experiments in which Eck fistulas were performed.

In all animals following Eck fistulas, marked reductions in estimated liver blood flow were recorded, approximating 50 per cent of the control volume. Although substantially reduced, this represents a somewhat larger volume flow than might be anticipated on the basis of deprivation of the liver of approximately 70 to 80 per cent of its blood source by diversion of the portal vein. Blalock and Mason reported the average contribution of the portal vein as 80.5 per cent of total liver blood flow, as opposed to 19.5 per cent contributed by the hepatic artery. Working with cats, Barcroft and Shore reported hepatic arterial contributions of 34 per cent. However, Grindley, Herrick, and Mann noted reversal of these flow relationships in two experiments. This suggests that some compensatory arterial flow may be anticipated under certain circumstances. Soskin and his associates stated that reversal of ordinarily accepted hepatic and portal flow ratios could occur. It is of interest to note, however, that a repeat estimation of liver blood flow 4 months after an Eck fistula on dog No. 49-149, Table IV, was considerably lower than that initially recorded in the postoperative animal.

Results following splenectomy.—Table V records the results of estimated liver blood flow (EHBF) before and after splenectomy. No consistent pattern is observed, as both in-

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TABLE IV.—ESTIMATED LIVER BLOOD FLOW, HEPATIC GLUCOSE PRODUCTION, AND SPLANCHNIC OXYGEN CONSUMPTION BEFORE AND AFTER ECK FISTULA

Controls					Following Eck fistula		
Dog	Weight kgm.	EHBF ml./min.	Glucose output mgm./min.	O_2 consumption splanchnic ml./min.	EHBF ml./min.	Glucose output mgm./min.	O_2 consumption splanchnic ml./min.
49–149	13.2	672	....	....	339	....	....
					202	27.2	9.85
51–58	12.9	749	31.4	15.8	334	39.6	9.70
51–29	15.4	922	43.9	10.5	439	56.6	15.70
51–36	12.5	564	25.3	26.7	374	48.4	9.97
51–24	10	403	30.5	24.3	234	25.5	13.40

creases and decreases in blood flow are recorded. This may reflect the effects of splenic engorgement under pentobarbital anesthesia in some instances in which extensive trapping of blood occurs. This may account for unknown variations in control values of splanchnic blood flow under pentobarbital anesthesia. The release of trapped red cells following splenectomy may produce increases in flow. These results appear inconclusive, possibly because of the selective influence of general anesthesia of this type on the spleen of the dog.

Glucose production. Estimated hepatic glucose production was calculated as the product of the hepatic-peripheral venous glucose difference (H-P) and the hepatic blood flow. Peripheral venous glucose levels were assumed to approximate closely the concentration of glucose in the portal vein. This seems justified, as the work of Bean and co-workers, Ravault and co-workers, and Sherlock and Walshe established no differences in glucose concentrations of portal anastomotic and antecubital venous blood in man.

Considerable variability in peripheral and hepatic venous glucose concentrations (H) was encountered, although hepatic levels remained consistently higher than the peripheral (P) samples. However, average figures for respective experiments are in general agreement. Similar variations were encountered in the animals studied following Eck fistulas. Glucose output in milligrams per minute was observed to vary from 17.8 to 94.7 milligrams of glucose per minute in the control group, with an average of 41.8. Following Eck fistula variation from 25.5 to 56.6 milligrams is noted with an average of 39.5 milligrams of glucose per minute. A marked increase in the hepatic peripheral venous glucose differences was recorded in the postoperative animals, these being in the neighborhood of twice the magnitude of the control group. It is to be noted, therefore, that no significant fall in hepatic glucose production occurred following Eck fistula.

Oxygen consumption. The average splanchnic oxygen consumption in the group of normal animals was found to be 25.3 milliliters per minute (Table I). This was calculated as the product of the peripheral arterial-hepatic venous oxygen difference and the hepatic blood flow. Variations from 10.5 to 35.6 milliliters of oxygen consumed per minute were recorded. However, average consumption for the control group is in close agreement with those reported by Blalock and Mason who found an average total splanchnic oxygen consumption of 23.8 milliliters per minute in a series of experiments.

A considerable reduction in splanchnic oxygen consumption was found following Eck fistula, the average consumption being 11.72 milliliters per minute. The magnitude of the reduction parallels the reduction in blood flow, being in the neighborhood of 50 per cent of the control values. This reduction was noted in all animals except 1 in which a reversal of these relationships was observed. On the assumption that almost all the hepatic blood flow following portal diversion is from the hepatic artery, the splanchnic oxygen consumption in the fasting state represents es-

sentially hepatic oxygen consumption. The oxygen consumption of the liver should not be altered theoretically by Eck fistula as the liver probably derives most of its oxygen from the hepatic artery. This is substantiated by the fact that the values of splanchnic oxygen consumption are reduced in the same order as liver blood flow following Eck fistula. However, it is impossible to state at this time whether this is a normal figure for hepatic oxygen consumption, because in normal control animals there is as yet no satisfactory way simultaneously to measure and separate hepatic arterial and portal venous blood flow.

TABLE V.—ESTIMATED HEPATIC BLOOD FLOW BEFORE AND AFTER SPLENECTOMY

Dog	Weight kgm.	Liver weight gms.	Spleen weight gms.	EHBF ml./min.	EHBF after splenectomy ml./min.
50–141	11.3	500	98	1010	758
50–164	10	370	82	713	999
50–165	12.7	434	75	540	874
50–166	14	...	87	1304	716
50–159	12.5	...	83	614	478
50–195	19.3	...	104	597	941

DISCUSSION

One is immediately impressed by the tremendous volume of blood flow associated with the portal system, as reflected by the estimated hepatic blood flow. The validity of this method appears well established. However, Cohn and co-workers have reported significant extrahepatic loss of dye, although this was not substantiated by Myers. Myers found similar concentrations for bromsulphalein in the inferior vena cava and the arterial blood in simultaneously drawn samples. Brauer using labelled S_{35} bromsulphalein, was able to recover quantitatively almost all labelled S_{35} from the liver, bile, and blood. Sherlock and co-workers have claimed extrahepatic loss of dye when the plasma bromsulphalein concentrations are below 1 milligram per cent. Although Myers was unable to corroborate this finding, all peripheral levels of bromsulphalein were maintained in the 1.0 to 5.0 milligrams per cent range in these experiments with few exceptions. The figures for estimated hepatic blood flow reported herein are somewhat higher than those reported in the published literature in which alternate methods of flow determination were employed. The effects of anesthesia upon the results obtained cannot be critically analyzed. Grindley, Herrick, and Mann, using the thermostromuhr, studied the effects of pentobarbital anesthesia on liver blood flow and found comparative elevations in flow volume in dogs while under anesthesia. The tremendous engorgement of the spleen under anesthesia may also play a contributory role in providing certain inaccuracies in flow volume. This is suggested by the results obtained before and following splenectomy, in which no consistent pattern was found. In any case, it can be concluded that under these circumstances the magnitude of hepatic blood flow is great and the comparative reduction following Eck fistulas significant. Bradley and associates, working with human cirrhotics, reported marked decreases (10 to 110 per cent) in hepatic blood flow following portal caval anastomosis.

The effect upon hepatic glucose production is of interest. A consistent increase in the peripheral-hepatic glucose difference was observed in the Eck fistula animals, and although there was considerable variation, the average P-H differences were approximately 80 per cent higher than those recorded in the control series. Presumably, this represents unaltered glycogenesis. This is reflected in the similar quantitative production of glucose in the control and Eck fistula animals. These results are slightly higher in the control group than those reported by Lipscomb and Crandall, who reported mean glucose output 27 milligrams per minute for dogs of comparable weight (121.8 mgm. glucose per kilo per hour).

Splanchnic oxygen consumption fell substantially in all but 1 animal in the postoperative period following Eck fistula. The arteriovenous oxygen differences also decreased somewhat, with 1 exception. The reduction in oxygen consumption was in the same range as the reduction of blood flow, indicating that there was probably little difference in liver oxygen consumption before or after Eck fistula. The fact that there was

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a slight decrease of the arteriovenous oxygen differences postoperatively under these conditions, may, therefore, indicate a slightly increased flow of oxygenated blood from the hepatic artery. This is also borne out by the fact that the reduction of blood flow is only in the range of 50 per cent, and theoretically at least, should be in the range of 75 per cent unless there is a corresponding increase in blood flow through the hepatic artery. It seems important that these relationships be properly evaluated in future experiments, as changes in blood flow and oxygen consumption may be related to the impaired protein synthesis in dogs with Eck fistula reported by Whipple.

CONCLUSIONS

1. Estimated hepatic blood flow, glucose production, and splanchnic oxygen consumption have been recorded in normal dogs and following Eck fistula.

2. Estimated hepatic blood flow before and after splenectomy have been recorded. These results appear inconclusive.

3. A reduction of approximately 50 per cent in the estimated hepatic blood flow occurred following Eck fistula.

4. Glucose production appears to be unaltered by Eck fistula.

5. Oxygen consumption fell following Eck fistula in all but 1 instance in the same range as the reduction in blood flow. This suggests that under these experimental conditions the liver is responsible for approximately one half of the total splanchnic oxygen consumption.

ADDENDUM: Since this paper was submitted for publication, the work of Werner and Horvath appeared in the *J. Clin. Invest.*, 1952, 31: 433–440, concerning the measurement of hepatic blood flow in normal dogs with bromsulphalein. Their similar findings in normal animals further emphasize the vagaries of the bromsulphalein method of measurement of liver flow, particularly when nembutal anesthesia is employed with an intact spleen.

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TECHNIQUE AND EFFECTS OF PORTACAVAL ANASTOMOSIS (ECK FISTULA)

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IT is the purpose of this paper to describe a simple method for anastomosing the portal vein to the vena cava. This method in modified form has been used by one of us (J. M.) since 1925, when it was first learned from F. C. Mann of the Mayo Clinic, and subsequently described by Fishback (1927). The other authors have had no difficulty learning it and have contributed to its elaboration as a definite technique. We use it constantly in our one stage technique for hepatectomy in the dog, described elsewhere. The operation has recently aroused considerable clinical interest as a technique for the treatment of portal hypertension in the final stage of hepatic cirrhosis.

The method depends upon the employment of a cutting thread as originally described by Fischler and Schroeder in 1909. In principle their operation consists of enclosing a silk cutting thread by 2 rows of sutures which form a watertight casement. When the suturing is complete, the cutting thread is seesawed backward and forward until it is delivered in the surgeon's hands. Subsequent descriptions of the method by Fishback, who described the Mayo Foundation technique, and by Markowitz have not altered the original principle of the method, although the procedure is speedier as the latter performs it. The commercial availability of vascular suture material in a convenient and an elegant form has made the operation simpler and of more practical value.

Dogs weighing approximately 12 kilograms are used. They are anesthetized either with intravenous nembutal or, when the operation includes hepatectomy, with intratracheal ether. A midline incision is made from the xiphoid to about 4 centimeters from the tip of the pubis. The gastrointestinal canal is gathered up and wrapped in the duodenal mesentery. The duodenum with its enclosed viscera is wrapped in a large warm Turkish towel and the package is lifted out of the peritoneal cavity and held motionless on the abdominal wall to the left of the midline. This maneuver clearly exposes the portal vein and the vena cava.

The portal vein is stripped of its overlying but not underlying coat of fascia for a distance of approximately 3 centimeters, depending on the presence of interfering tributaries and the size of the animal. For a dog weighing 12 kilograms, which is most suitable, 3 centimeters will be ample. If the vein is not dissected from its fibrous bed in the gastrohepatic omentum, there will be little danger of suturing the vein in an occlusive fashion since approximately half the lumen will be free. The size of the portal vein ensures a large margin of safety, and if no more than half of it is involved in the suturing there will be no back pressure.

As a first step an untied ligature, made of fishing reel line, is introduced about the portal vein definitely on the hepatic side of the last tributary. This is of course, left untied until the Eck fistula has been performed. Two stay sutures of No: 000 silk or, preferably, of equally fine nylon, are placed so as to align the portal vein to the inferior vena cava. It is the duty of the assistant to hold these structures in apposition while the stay sutures are placed. These sutures are passed through the opposing walls of both veins, generally at the extreme ends of the portion of the freed portal vein. The upper stay suture should be about 2 centimeters from the bifurcation of the portal vein. When both stay sutures have been placed, the needle of the bottom suture, using a Rankin clamp as a needle holder, is used for laying the posterior suture line.

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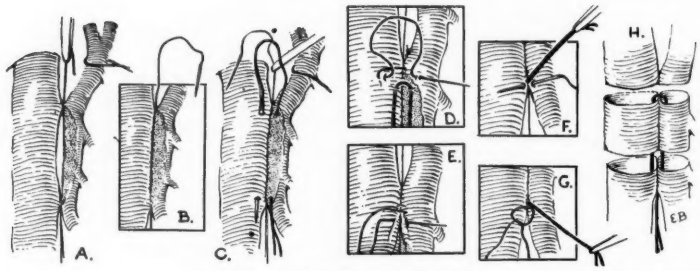

Fig. 1. Details of Eck fistula.

During this part of the operation the assistant rotates the portal vein somewhat so that the suture line is dorsal to the apposed surfaces of the two vessels. The bites should not be too far apart. When the top suture has been reached, a tie is made and 1 needle is removed. The other one is temporarily tucked out of the way.

A cutting suture is now inserted close to the suture line. It consists of a 3 centimeter fine needle (No. 9) threaded with button-hole silk twist which has been autoclaved in mineral oil with the rest of the linen. It may be autoclaved only once as the needle loses its temper and the silk becomes weakened. The needle is inserted as illustrated (Fig. 1). The point is carefully seized and the needle is withdrawn in a direction exactly continuous with that of its insertion until, if necessary, it is embedded in the liver. The attached suture is gently pulled through to prevent sawing a hole in the portal vein. This maneuver is now repeated from above down into the vena cava, this being a less hazardous procedure owing to the tough walls of the large vein. The cutting suture is carefully drawn taut and the ends are laid aside in such a manner as to prevent their becoming twisted. The casement about the cutting suture is now completed by laying the anterior suture line, using the needle of the cephalic stay suture. The angle is carefully closed, the first bite in the anterior suture line being in the vena cava. The suture line must at all times be taut. Naturally the suture line must not include the cutting thread, and when this happens it is due to carelessness. When the emerging ends of the cutting suture have been reached, the suturing is continued around them in such a way as to form a snug purse-string effect. The anterior suture line is tied *snugly* to the bottom stay suture.

The surgeon now lifts the ends of the cutting thread, sawing it free by smooth traction on alternate ends. The two hands should be almost touching to prevent sawing a hole in the portal vein. If the threads do not pull freely, they have been caught in the suturing. As soon as the cutting suture is free there may be a small welling of blood from the point of exit; if this is so it is controlled by the tip of the finger and it stops as soon as a single interrupted stitch is placed. This is most unusual if the suturing has been snug.

In four fifths of the cases the actual Eck fistula can been completed in 12 minutes without mishap and without the loss of more than 5 cubic centimeters of blood. The previously placed ligature around the portal vein is now tightly tied. The portal vein immediately becomes full but there should be no cyanosis of the bowel.

The mortality is negligible, and thrombosis is most unusual. Once learned the operation is simple. It is quicker than methods recently described (2, 5) which involve the use of clamps, since these instruments do not obviate the need for suturing the two veins together. Moreover, the suturing here used is much more secure.

Should this operation come to be used in the human, it is obviously wiser to employ interrupted sutures as originally described by Fischler and Schroeder.

DISCUSSION

It is an odd thing that ligature of the portal vein with diversion of the portal blood stream to the inferior vena cava is followed by so little

physiological disturbance. Even when the animals are fed meat, they tolerate this well. For years the classical view has prevailed that when animals with an Eck fistula are fed meat they usually fare badly and often die following mysterious convulsions (Freeman 1949). This sequence is unusual, though we have seen it. In fact, our animals have been so remarkably well that one feels called upon to explain the convulsions reported by other workers in this field. We have nothing but speculation to help us but we believe that possibly the prolonged nature of the operation in the early days, well over 2 hours, or the use of clamps may have resulted in considerable fibrosis of the structures about the portal vein, with partial obliteration of the hepatic arteries. Freeman (1949) reported that meat intoxication was often produced in Eck fistula dogs by feeding them 50 grams per kilogram of raw ground horse meat daily. It was often necessary to force feed them, in which case the diet was more completely retained if fed in divided doses. We can confirm that such dogs often refuse these huge rations and merely nibble at them. Possibly this is why our animals only exceptionally develop symptoms of intoxication. A more significant thing is Freeman's observation that complete ligation of the portal vein (in 2 stages) resulted in meat intoxication in only 1 dog out of 5; this animal was twice presumed to be dying but recovered spontaneously and resumed eating meat without signs of intoxication even though the quantity it consumed was doubled. Ligation of the portal vein is an operation that is done quickly and with little disturbance to the other structures about the vein. As a result there is less postoperative fibrosis. The liver of such a preparation shows less histological changes, and the dye clearance test shows less marked and less consistent retention than in Eck fistula dogs. In fact, Freeman states that the lowest values for dye excretion in Eck fistula dogs *"were usually not obtained immediately after operation; therefore, it is reasonable to suppose that secondary changes occurring in the liver contribute to the loss of excretory function for the dye."*

Our remarks about the relative innocuousness of an Eck fistula are prompted by the paper of Large and Preshaw who also report that after operation the animals lived normally and tolerated various diets without ill effect. Whipple and co-workers have shown that Eck fistula animals can live in good health for as long as 8 years. However, their studies showed that when placed under the strain of anemia or hypoproteinemia these animals fail to regenerate hemoglobin and plasma protein as efficiently as normal dogs. The convulsive state that supervenes terminally in the liverless dogs (24 to 30 hours) after hepatectomy resembles clinically that which is seen in meat intoxication in the Eck fistula animals. The dog appears to be blind, with his muzzle propped against the corner of the cage; the muscles are spastic and tremulous, breathing is rapid, and when convulsions occur, they are extremely violent. Possibly they have a similar chemical basis, the accumulation of a substance that is metabolized by the liver.

SUMMARY

A simple technique for performing an Eck fistula is brought up to date in the light of the availability of blood vessel sutures in surgical supply shops. The technique does not require clamps, is speedy, safe, and accurate. It is based upon the use of a cutting thread, originally described by Fischler and Schroeder, used many hundreds of times by F. C. Mann of the Mayo Foundation, who taught the method to Fishback and to one of us, and subsequently used by us with slight modifications over a period of 25 years. Anyone who takes the trouble to learn the method will prefer it to others. It could have a direct clinical application. The great majority of Eck fistula dogs show no physiological disturbance under ordinary conditions of laboratory housing.

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A COMPARISON OF CECOSTOMY AND TRANSVERSE COLOSTOMY IN COMPLETE COLON OBSTRUCTION

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THE surgical management of the distended abdomen with complete large bowel obstruction is a serious problem. An important decision to be made is whether to do a cecostomy or a transverse colostomy as an emergency decompression procedure. Some surgeons recommend exploration and transverse colostomy. A minimal procedure such as tube cecostomy is advised by others.

With this problem in mind the authors have reviewed all cases of acute large bowel obstruction admitted as emergencies on the general surgical services at the Los Angeles County General Hospital during the period 1948 to 1950. There were 240 such cases. Emergency operative procedures were employed for decompression in 146 patients. There were 34 cecostomies and 57 transverse colostomies done. The 34 instances of cecostomy have been evaluated as to risk, and a comparable group of 34 instances of transverse colostomy have been selected for comparison.

The etiology of obstruction in the 240 cases is presented in Table I. The "miscellaneous" group included such conditions as rectal stricture, carcinoma of the cervix, megacolon, embolus to the celiac artery, adhesive bands strangulating the cecum, carcinomatosis, endometriosis, pelvic abscess, and carcinoma of the bladder with pelvic extension. As would be anticipated, cancer of the colon comprised 42 per cent of the total cases. Carcinoma involved the left half of the colon 3 times as frequently as the right. The "unknown etiology" group included patients who left the hospital before diagnostic studies could be completed. It is of interest to note that volvulus of the sigmoid in this series was 8 per cent. Only those cases of diverticulitis of the colon were included in which obstruction was the main problem. Abscess formation occurred in approximately half of the group with diverticulitis.

The emergency operations performed for these obstructions are listed in Table II. The "miscellaneous" group included exteriorization of the sigmoid, closure of a colon perforation, ileosigmoidostomy, colostomy revision, left colon resection, and appendicostomy. Ileotransverse colostomy was usually performed in obstructing cecal lesions. Most of the sigmoid resections were in patients who had volvulus of the sigmoid.

For a critical study of this problem it was especially important that a comparison be made of cecostomy and transverse colostomy in patients who had the same severity of illness. This was possible since the larger number of cases of transverse colostomy permitted a choice of those presenting risk similar to the cases of cecostomy. The criteria for comparison included the age, nutrition, and degree of anemia, associated diseases, the duration and severity of obstruction, as well as the fluid and chemical balance. The type of anesthesia was also used to grade these pa-

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TABLE I.—ETIOLOGY OF COLON OBSTRUCTION

Etiology	No. of cases
Cancer of the left colon	75
Fecal impaction	34
Cancer of the right colon	25
Volvulus of the sigmoid	20
Diverticulitis of the colon	18
Diverticulitis of the colon with perforation	16
Colostomy stricture	9
Perforation of the colon with abscess formation	5
Volvulus of the cecum	4
Miscellaneous	15
Unknown etiology	19
Total	240

TABLE II.—OPERATIONS PERFORMED FOR THE RELIEF OF OBSTRUCTION

Type of operation	No. of cases
Transverse colostomy	57
Cecostomy	34
Ileotransverse colostomy	15
Sigmoid resection	14
Exploration only	8
Sigmoid detorsion	4
Right colectomy	3
Transverse colon resection	2
Ileostomy	2
Miscellaneous	7
Total	146

tients, since many were so ill that local block anesthesia was all that could be given. The average age of the patients with cecostomy was 67 while of those with a transverse colostomy it was 68 years. The severity of illness in these elderly patients with obstruction is attested to by the fact that 76 per cent were very poor risks!

The relation between mortality and effectiveness of decompression in the patients studied is shown in Table III. As noted, the mortality in obstruction treated by cecostomy was 56 per cent compared to 23.5 per cent when treated by transverse colostomy. Dennis[1] has reported a mortality of 7.9 per cent with transverse colostomy as against 50 per cent with cecostomy. The effectiveness of decompression is of great importance in evaluating these procedures. The obstructive state must be immediately and adequately corrected or the patient will die. Decompression was considered satisfactory if the distention was relieved within 48 hours following surgery. This occurred in 53 per cent of the cecostomy cases and in 85 per cent of the transverse colostomy cases. Decompression was considered unsatisfactory if the abdominal distention could not be relieved by the operative procedure chosen. This was found to occur in 33 per cent of the patients with cecostomy and in 3 per cent of those with a transverse colostomy. Questionable decompression occurred 4 times in each type of procedure. One transverse colostomy and 4 cecostomies were eliminated from tabulation because of death within the first 24 hours. The ileus associated with perforation and peritonitis and the atony from overdistention and malnutrition were found to influence the effectiveness of decompression even though the surgery was adequate.

A further study of the mortality in relation to decompression was made in Table IV. If one eliminates cases of perforated colon and blind tube cecostomy the mortality was still 36 per cent with cecostomy as compared to 16 per cent with transverse colostomy. The decompression was satisfactory in 64 per cent with cecostomy as compared to 92 per cent with transverse colostomy.

Comparing the two procedures in patients with perforated bowel there was a mortality of 62.5 per cent with cecostomy and of 44 per cent with transverse colostomy, and satisfactory decompression of 43 per cent with cecostomy and of 67 per cent with transverse colostomy. The so-called "blind tube cecostomy" gave a mortality of 75 per cent with a satisfactory decompression in 44 per cent.

In order of frequency the factors that contributed to death in the cecostomy cases were: inadequate decompression, perforation of the cecum, missed diagnosis, pulmonary and cardiac complications, chemical imbalance, and perforation of the sigmoid.

Technical errors that contributed to the cecostomy deaths were: inadequate exteriorization of the cecum, failure to mobilize the cecum sufficiently to prevent tearing or retraction of the bowel, inadequate fixation of the cecum causing retraction and closure of the cecostomy, failure to irrigate the cecostomy tube adequately, and too long delay in opening the cecum after operation.

The causes of death in the instances of transverse colostomy include cardiac and pul-

[1] DENNIS, C. Treatment of large bowel obstruction. Surgery, 1944, 15: 713–734.

TABLE III.—EFFECTIVENESS OF DECOMPRESSION AND MORTALITY

	Cecostomy	Transverse colostomy
Satisfactory, No.	16 (53%)	28 (85%)
Unsatisfactory, No.	10 (33%)	1 (3%)
Questionable, No.	4	4
Deaths within 24 hours, No.	4	1
Total No.	34	34
Mortality, per cent	56	23.5

monary complications, perforated sigmoid with peritonitis, renal failure, and a missed perforated cecum.

The technical errors contributing to death in the transverse colostomy patients were: inadequate mobilization of the colon, torsion of the colon in exteriorization, too tight wound closure resulting in edema and low grade infection, too long delay in opening the colostomy, and removing the colostomy support too soon to permit retraction of the bowel.

Mortality resulting from closure of the cecostomy or transverse colostomy was not a factor since there were no deaths in surgical closure of either. The closure of a cecostomy is ordinarily considered to be an easier surgical procedure than the closure of a transverse colostomy.

DISCUSSION OF ILLUSTRATIVE CASES

The following case reports have been selected for presentation because they are representative of accepted surgical therapy or of mistakes which may be encountered.

Perforation of the Cecum with Cecostomy

CASE 1. No. 1208–268, a 64 year old man, had had complete obstruction for 4 days prior to hospital entry. He was noted to be dehydrated and to have a markedly distended and tense abdomen. Peristalsis was active with high pitched peristaltic rushes. There was a palpable rectal mass. At surgery, carcinoma of the rectum was found, and further exploration revealed a gangrenous perforated cecum with peritonitis. Immediate decompression of the colon was carried out, as well as exteriorization of the cecum. A cecostomy opening was made with cautery on the second postoperative day. Decompression was recorded as satisfactory. Three weeks later the patient underwent abdominal-perineal resection for a grade II adenocarcinoma of the rectum.

Perforation of the cecum is an absolute indication for exteriorization and cecostomy. In the case under discussion we believe that the immediate surgical decompression of the colon plus complete exteriorization of the cecum with prompt opening postoperatively resulted in this uneventful recovery.

Cecostomy for Obstruction at the Hepatic Flexure

CASE 2. No. 744–396, a 37 year old cirrhotic, was admitted with a 2 weeks' history compatible with partial obstruction and a 4 day history of abdominal cramps, vomiting, and absence of bowel movements. His abdomen was noted to be moderately distended and a right lower quadrant mass was visible when the patient complained of abdominal cramps. At surgery he was found to have an obstruction of the colon at the hepatic flexure, due to a tumor arising in the right lobe of the liver. Because of associated severe small bowel distention with fluid, immediate surgical decompression of the ileum was done with suctioning of small intestinal contents. The cecum was exteriorized and a large mushroom catheter was inserted for decompression. Two days later the cecum was opened with cautery, and the patient recovered from this emergency procedure with no complications.

It was believed that in this case suctioning of the small bowel, combined with an exteriorized cecostomy, employing a large catheter for decompression, and prompt opening of the cecostomy, hastened recovery. Obstructing lesions of the hepatic flexure are best treated with cecostomy.

Transverse Colostomy for Carcinoma of the Sigmoid

CASE 3. No. 823–033, a 68 year old woman, had noted low grade obstructive symptoms of 2½ months' duration and had had complete obstruction with vomiting for 12 days. She had marked abdominal distention with high pitched bowel sounds. A preoperative barium enema demonstrated an obstructing sigmoid lesion. Her blood chemistries revealed an extremely low potassium. She was given preoperative potassium and blood, and a transverse colostomy was performed as an emergency decompression procedure. The colostomy was opened on the third postoperative day with good decompression and an uneventful recovery.

This patient demonstrates that even though there is a severe electrolyte imbalance, prompt replacement therapy together with adequate immediate decompression of the obstruction can result in early recovery of the patient.

Transverse Colostomy for Ruptured Diverticulum

CASE 4. No. 451–195, a Caucasian male, aged 53 years, presented the picture of acute peritonitis.

He complained of abdominal pain, and absence of bowel function of 2 days' duration. His temperature was 101 degrees F. and his abdomen was markedly distended, tender, and rigid, and there was a left lower quadrant mass. The white blood count was recorded as 18,400 (87 per cent polymorphonuclears), and emergency roentgenograms showed large and small bowel gas under no tension. Following the administration of antibiotics and an adequate period for hydration the patient was taken to surgery, where exploration revealed a perforated sigmoid diverticulum with early abscess formation. A transverse loop colostomy was done and later opened on the second postoperative day. Decompression was satisfactory and recovery uneventful except for a temporary ileus, secondary to the peritonitis. The colostomy was closed 3 months later, following a normal barium enema.

A transverse colostomy provides decompression as well as complete fecal diversion, which cannot be obtained by cecostomy.

Tube Cecostomy without Exploration, Resulting in Inadequate Decompression and Perforation of the Cecum and Transverse Colon

CASE 5. No. 1125-646, a 67 year old Caucasian man, entered the hospital with an 8 day history of acute obstruction, with fecal vomiting and absence of bowel movements. He was noted to be severely dehydrated and had a markedly distended tender abdomen. Peristalsis was hypoactive and tinkling in nature. A preoperative barium enema showed a complete sigmoid obstruction. The patient was taken to surgery, and a tube cecostomy without exploration was performed. The cecum was not mobilized. However, a large dePezzer catheter was inserted for continued decompression. The catheter was irrigated 4 times daily, but fecal drainage was charted as poor and the patient remained distended. Despite antibiotics and adequate supportive therapy he developed peritonitis and expired 3 days following surgery. At postmortem examination the cecum was still distended with feces, and it was not noted that there had been leakage of bowel content around the catheter within the abdomen. There was an area of gangrene on the cecum and two gangrenous patches on the transverse colon with perforation.

It is believed that the cecostomy tube was inadequately irrigated in this case. Aspiration of the bowel at surgery, followed by exteriorization of the cecum, would have resulted in better decompression. The emptying of the colon through a small cecostomy opening is all too frequently inadequate and disappointing. A transverse colostomy would have been preferable in this case.

TABLE IV.—EFFECTIVENESS OF DECOMPRESSION AND MORTALITY WITH CECOSTOMY AND WITH TRANSVERSE COLOSTOMY

	Total No. cases	Mortality per cent	Satisfactory decompression per cent
Cecostomy—exteriorized type (eliminating tube cecostomy, perforated cecum and sigmoid)	14	36	64
Transverse colostomy (eliminating perforated cecum and sigmoid)	25	16	92
Cecostomy—exteriorized type in perforation of cecum and sigmoid	8	62.5	43
Transverse colostomy in perforation of cecum, sigmoid, and rectum	9	44	67
Tube cecostomy without exteriorization	12	75	44

Transverse Colostomy with Perforated Cecum Missed at Surgery

CASE 6. No. 590-024, a 75 year old Caucasian female, gave a history of having noted abdominal pain, distention, and vomiting for 10 days prior to admission. She had melena and an unexplained weight loss of 25 pounds. On examination her temperature was 100.8 degrees F. and her pulse was 100. There was marked abdominal distention, tenderness, and peristaltic sounds were high-pitched and tinkling. Laboratory reports showed a white blood count of 16,400 with 84 per cent polymorphonuclears. A preoperative diagnosis of neoplasm of the descending colon with obstruction was made. At surgery, free air was noted on opening the peritoneum. The cecum was inadequately visualized and the site of perforation was not found. The obstruction lesion was carcinoma of the sigmoid colon, and a transverse colostomy was performed. Using cautery, the colostomy was opened 4 days following surgery. The patient developed congestive failure and died on the fifth postoperative day, and autopsy revealed a perforated cecum with generalized peritonitis.

In retrospect, the presence of free peritoneal air should have caused suspicion of perforation of the cecum, and an exteriorized cecostomy should have been performed instead of the transverse colostomy. A perforated cecum, as previously mentioned, is an absolute indication for cecostomy. Delay in opening the colostomy was undoubtedly an additional factor in inadequate decompression in this case.

Tube Cecostomy without Exploration for Volvulus of the Sigmoid

CASE 7. No. 1116-777, a 72 year old man, had experienced abdominal cramps for 3 days and vom-

iting for 2 days. The abdomen was markedly distended, and there was high-pitched hypoactive peristalsis. A tentative diagnosis was made of obstruction secondary to carcinoma of the left colon. At surgery the cecum was noted to be massively distended and, because of the critical condition of the patient, a tube cecostomy was performed without exploration of the abdomen. The patient did poorly and expired some 5 hours later. At autopsy the patient had a 180 degree volvulus of the sigmoid, without vascular changes of the bowel. The large and small intestine were distended with gas.

This case represents one of the pitfalls encountered when a tube cecostomy is done without exploration. Volvulus of the sigmoid is not an uncommon cause of complete large bowel obstruction and demands specific treatment rather than a cecostomy or transverse colostomy. A preoperative barium enema is helpful in the diagnosis of volvulus of the sigmoid.

Tube Cecostomy for Sigmoid Carcinoma with Inadequate Decompression

CASE 8. No. 198-809, a 76 year old woman, had noted rectal bleeding of 2 months' duration and abdominal cramping pain associated with obstipation for 1 week. On examination she was noted to have marked abdominal distention, visible peristalsis, and high-pitched tinkling peristaltic sounds. She had a 3 plus urinary acetone. Following preparation with intravenous fluids and penicillin, the patient was taken to surgery, where a sigmoid carcinoma was found to be causing large bowel obstruction. A tube cecostomy, with partial exteriorization of the cecum, was done for emergency decompression. Following operation the patient continued to be distended, despite cecostomy irrigations. On the sixth postoperative day the tube was removed, the cecum retracted, and the cecostomy closed. A second tube was inserted, and 2 days later the patient died of a massive pulmonary embolism. At autopsy it was noted that the ascending and transverse colon were still distended.

Adequate initial mobilization and exteriorization would have prevented retraction and spontaneous closure. This case also demonstrated the difficulty of adequately decompressing the colon through a tube cecostomy. A transverse colostomy would have been a more desirable procedure in this case.

Perforated Sigmoid Diverticulum Treated with Cecostomy

CASE 9. No. 1176-110, a woman, aged 63 years, entered the hospital with a 1 day history of abdominal pain, vomiting, and obstipation. Her abdomen was markedly distended with generalized tenderness and absent peristalsis. The white blood count was 34,000 with 90 per cent polymorphonuclears, and an emergency barium enema revealed a sigmoid obstruction. At surgery a positive diagnosis could not be made, due to local inflammatory reaction. However, a tentative diagnosis of carcinoma of the sigmoid colon was made and an exteriorized cecostomy performed for decompression. Following this operation the patient did poorly because of persistent distention and inadequate fecal diversion. For this reason a second operation was done, at which time it was ascertained that the pathological process present was a ruptured sigmoid diverticulum. At this operation obstructing inflammatory adhesions were severed. One week later the patient expired with a massive pulmonary embolus.

The failure to recognize the perforated lesion of the sigmoid led the surgeon to perform an inadequate procedure. A cecostomy does not divert the fecal stream, and a transverse colostomy should have been done.

SUMMARY

Surgery is often too long delayed in complete obstruction of the colon. Expectant treatment with suction and enemas is hazardous in large bowel obstruction, since in the majority of cases obstruction is of a closed loop type due to a competent ileocecal valve. Delay results in a more critically ill patient and the likelihood of cecal perforation; such perforation was noted in 10 of the 146 patients undergoing operation in the present series. A flat plate of the abdomen and an emergency barium enema are roentgenologic procedures that aid in proper diagnosis.

Exploration, even though limited in certain cases, will obviate a missed diagnosis. Six deaths in this series were due to unknown causes of obstruction. Included were 2 patients with volvulus of the sigmoid who were treated by cecostomy. One patient with a perforated cecum was unsuccessfully treated by a transverse colostomy.

Decompression of a severely distended bowel at the time of surgery not only improves the patient's chance of surviving but also makes the surgeon's work easier.

In this study the tube cecostomy proved to be an inadequate emergency decompressing procedure. An exteriorized cecostomy was

better. When there is a choice of procedures a transverse colostomy results in lower mortality, more effective decompression, less tendency to chemical imbalance, and earlier and better preparation of the colon for subsequent surgery. However, an exteriorized cecostomy is indicated in cases of perforations and partial gangrene of the cecum. It is also recommended for complete obstruction involving the ascending colon, hepatic flexure, and transverse colon.

A transverse colostomy is recommended in diverticulitis of the left colon with complete obstruction and perforation, and in complete obstructions of the rectum, sigmoid, and descending colon (other than volvulus).

Local anesthesia in poor risk patients, judicious use of blood transfusions, correction of chemical imbalance, and the use of antibiotics have made possible a more aggressive surgical approach in the presence of acute colon obstruction.

EXPERIENCES WITH HIP PROSTHESES

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INCREASED interest has been shown in hip prostheses since a certain measure of success has been achieved by their use. According to established concepts, the utilization of foreign material to replace a portion of a joint is unphysiologic. At a recent combined meeting of the Robert Jones Society and the Orthopedic Guild in Cleveland, two of the authors were privileged to hear this question discussed by several more experienced and wiser men than we. Some were quite vehement in their opposition to hip prostheses and declared their use unphysiologic. With this we must agree, on the basis of the fundamental principles in which we have been trained. However, the difference is slight between the prosthesis and the vitallium cup which has been used so successfully for arthroplasties. More and more, with the development of inert metal, it has been found that certain materials can be used successfully within the body without ill effect. One can remember when Lane and Sherman were held in ridicule for their insistence upon the advantages of plates and screws for the internal fixation of fractures. The use of the intramedullary nail is certainly meeting with some success in various parts of the world and, on the surface, this would appear more unphysiologic than anything we have known to date. Thus, we must assume that there are certain situations in which, no matter how unphysiologic it may seem, there are advantages that can be obtained by the use of some forms of foreign materials within the body.

At present, there are about 40 to 50 different types of prostheses being manufactured. Just which ones will survive the test of time remains to be seen. Some of the metallic prostheses are quite heavy, and it would appear to us that this would be a decided disadvantage. The ideal requirements for a prosthesis to be considered are the ease of insertion or extraction, simplicity of construction, proper distribution of stress and strain, and stability and durability of the artificial head. From the number and variety of prostheses now being manufactured, it is obvious that none has been found to meet all the necessary requirements.

We wish to submit a report concerning the types of hip prostheses that we have used in a group of 17 patients. We recognize that in making this report the length of follow-up has been altogether too short. Perhaps one of the greatest disadvantages will prove to be the eroding effect of the constant contact of inert material against bone. To date, however, we have not encountered this complication. The advantage of a prosthesis which appeals to us is that of its use in elderly patients of 75 years or over, whom it is necessary to ambulate quickly and whose convalescence must be shortened as much as possible in order to avoid the complications that go with old age. So many of these patients cannot be relied upon not to bear weight on a fractured hip which has been nailed or fixed with some other means of internal fixation. As a result, many nails, blade plates, and the like have cut through necks of femurs or have worked their way out. Perhaps in some cases it has been the fault of the operator. We concede, in cases of acute fractures of the neck of the femur, that an adequately fixed nail with plate attachment is probably the method of choice in a patient who can be up in a chair or wheelchair and can be trusted not to bear weight on the involved leg for at least a 3 month period. Other procedures, such as osteotomies and reconstructions must also depend on either external or internal fixation. With the prosthesis a patient can usually be placed in a wheelchair within the first week following operation. Within 2 to 3 weeks, the patient can be up on crutches. One need not concern oneself whether the patient voluntarily or involun-

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tarily bears weight on a properly placed appliance. We will report on 17 cases, stressing the complications encountered and the end result, and draw certain conclusions based on this study.

CASE REPORTS

CASE 1. V.B., aged 80 years, was admitted to the hospital on April 10, 1951, operated upon April 13, 1951, and discharged on May 19, 1951. The diagnosis was a 1 month old fracture of the neck of the left femur, intrascapular with malposition. Operation consisted of replacement by a Judet acrylic head. The patient was up in a chair on April 30, 1951. She had no complaints and was doing well in a parallel walker by May 8, 1951. She was to have crutches or a cane on May 12, 1951, and was doing better than expected. The patient had a moderate degree of pain in the left hip for several days after operation. On the whole, however, she had an uneventful convalescence. Check-up roentgenogram of the Judet prosthesis showed satisfactory position. Three months following operation the patient was walking with a cane and a moderate limp. She stated that she had been out frequently for various social affairs but that on walking any distance had pain in the hip and anterior portion of the thigh. She was last seen on January 26, 1952, and was doing moderately well.

CASE 2. G.F., aged 64 years, was admitted to the hospital on July 26, 1951, operated on July 28, 1951, and was discharged on September 15, 1951. The diagnosis was old, ununited fracture of the neck of the right femur, and the operation consisted of replacement of the right femoral head with a Judet acrylic prosthesis. The patient was up in a wheelchair on August 10, 1951, and on August 12, 1951, was using crutches and active exercises to the right leg, except external rotation. Her hospitalization was prolonged because she was a widow who had no means of domiciliary care. She had a satisfactory postoperative convalescence, was walking well, and had no complaints. On October 19, 1951, she had approximately 75 per cent of normal hip motion, and we have not seen her since that time but recent inquiry revealed that she gets around in her own home with the use of a cane. She complains of pain on overuse of her hip and has a moderate limp. We believe that her prognosis is good.

CASE 3. R. W., aged 79 years, was admitted to the hospital on June 15, 1951, operated on June 19, 1951, and was discharged on July 5, 1951. The diagnosis was fracture of the neck of the left femur and fracture of the surgical neck of the left humerus. The operation consisted of excision of the left femoral head and replacement with a Judet acrylic prosthesis. The patient was up in a wheelchair for short intervals on June 27, 1951, and was discharged on July 5, 1951, with no complaints, returning to her home by ambulance. She had a satisfactory convalescence following the operation and closed reduction of the fractured shoulder. The patient was walking well with a cane on October 20, 1951, and examination at that time revealed that her legs were equal in length and flexion and abduction were limited to 20 degrees. She complained of slight soreness in the anterior aspect of the thigh. The patient has not been seen since that time but her daughter has reported that her mother is getting around well in her home. She is still using a cane and cannot be on her feet for long periods of time but she is able to get out for relaxation occasionally. The daughter states that her mother seems satisfied with her progress to date.

CASE 4. H. S., aged 72 years, was admitted to the hospital on October 31, 1951, operated on November 3, 1951, and was discharged from the hospital on December 11, 1951. The diagnosis was acute fracture of the neck of the right femur. The operation consisted of excision of the right femoral head with insertion of a Judet type metallic prosthetic head. On November 17, 1951, the patient was able to balance herself and walk a few steps on crutches with help. At the time of her discharge, following a satisfactory convalescence, her husband died in another hospital and in an effort to be with him during his last days she walked considerably. It was also necessary for her to be on her feet for long periods of time during the funeral and, as a result, when she was seen on December 21, 1951, the patient complained of considerable pain on weight bearing. The hip was fairly limited at that time and she was advised to rest more than she had been able to previously. On January 17, 1952, she had only slight discomfort in her hip and was able to walk with a cane and a slight limp. When last seen on February 20, 1952, she had no limp when walking with a cane but complained of some pain in the anterior aspect of the thigh.

CASE 5. G.T., aged 49 years, was admitted to the hospital on November 22, 1951, operated on November 24, 1951, and was discharged on December 23, 1951. The diagnosis was transcervical fracture of the right femur and old left hemiplegia secondary to a cerebrovascular accident. The operation consisted of excision of the right femoral head and replacement with a Judet acrylic prosthesis. On December 4, 1951, it was necessary to perform a closed reduction of a postoperative dislocation of the prosthesis of the right hip. On December 6, 1951, the sutures were removed and the wound healed. On December 16, 1951, the boot cast which had been applied to prevent external rotation was removed. The patient was discharged on December 23, 1951, returning to her home by ambulance to be further cared for by her local doctor. It was felt that her prognosis was bad but the type of operation was selected because of the hemiplegia, in order to facilitate nursing care and allow her to return home as soon as possible. Her local doctor has reported no change since her discharge although dislocation of the hip has not recurred and she does not have any discomfort in the right hip.

CASE 6. J.K., aged 63 years, was admitted to the hospital on June 22, 1951, operated on June 25, 1951, and was discharged on August 16, 1951. The diagnosis was intrascapular fracture of the right hip joint and dislocation of the right hip anteriorly and medially. Operation consisted of removal of the head of the femur and application of an acrylic prosthesis to the head of the femur. The patient was discharged from the hospital on crutches and when seen on February 1, 1952, was walking with only moderate discomfort, and we felt that a satisfactory result had been obtained. The prognosis in this case is good.

CASE 7. G.P., aged 75 years, was admitted to the hospital on April 14, 1951, operated on April 18, 1951, and discharged on May 19, 1951. The diagnosis was ununited fracture of the neck of the left femur and the operation consisted of reconstruction of the head of the left femur and insertion of an acrylic head. The patient was up in a wheelchair on May 15, 1951. At the time of her discharge from the hospital she had good motion and had had little postoperative pain. She was still not bearing weight at that time but it was believed that her prognosis was good. She was last seen on January 25, 1952, at which time her pain had subsided entirely and her condition was very good except for some back discomfort caused by arthritis which had no relation to her hip. This patient had an excellent result with the prosthesis.

CASE 8. H.S., aged 53 years, was admitted to the hospital on October 11, 1951, operated on December 20, 1951, and was ready for discharge from the hospital on February 12, 1952, but was detained because of other medical conditions. The diagnosis was old nonunion of a fracture of the neck of the right femur. At the time of his admission roentgenograms demonstrated a subcapital fracture of the right femur. Shortly after his admission the patient had acute thrombophlebitis with pulmonary infarcts, and therefore surgery had to be postponed until December 20, 1951. When he was ready for discharge on February 12, 1952, he was ambulatory on crutches with almost complete weight bearing and he was entirely free of pain in his hip.

CASE 9. H.C., aged 55 years, was admitted to the hospital on October 28, 1951, operated on November 1, 1951, and was discharged on November 19, 1951. The diagnosis was nonunion of a fracture of the neck of the left femur. The operation consisted of arthrotomy of the hip joint, excision of the head of the femur, and replacement with a Judet metallic prosthetic head. The patient started to walk with crutches on November 13, and was discharged with crutches. On December 29, 1951, examination revealed that he had flexion of 90 degrees, 50 per cent rotation, and 30 per cent abduction of the left hip. There was ¼ inch shortening of the left leg and the patient complained of slight pain in the left knee. On January 19, 1952, the range of motion was the same. The quadriceps on the left was poor and there was a complaint of soreness in the groin, particularly with changes of weather. The patient was still using a cane and walking with a moderate limp, but seemed happy with the result. We believe that the prognosis is good.

CASE 10. M.S., aged 60 years, was admitted to the hospital on May 31, 1951, operated on June 4, 1951, and discharged from the hospital on August 11, 1951. The diagnosis was ununited fracture of the neck of the right femur. The operation was a Judet arthroplasty of the right hip, with insertion of an acrylic femoral head. On June 11, all sutures were removed and the patient was up on crutches on July 3, 1951, without bearing weight on the right foot. The patient was discharged on August 11, 1951, to a convalescent home, at which time she was bearing weight satisfactorily. At the time of examination in January, 1952, the patient was bearing weight without crutches and all pain was rapidly subsiding. This patient had a good result and we believe that the prognosis is good.

CASE 11. E.C., aged 75 years, was admitted to the hospital on September 5, 1951, operated on September 8, 1951, and was discharged on October 2, 1951. The diagnosis was intertrochanteric fracture of the left hip. Operation consisted of replacement of the head and neck of the left femur with a McBride prosthesis. The postoperative course was good except for the development of a hematoma in the wound which was drained and at the time of discharge the drainage area was almost completely healed. At the time of discharge the patient was ambulatory with partial weight bearing and practically no discomfort. On December 5, 1951, the wound was healed and the patient was doing well with a complete range of motion and only needed to use a cane at home. There were only minimal complaints when she was examined by her local doctor who reported satisfactory progress since our last examination. The prognosis in this case is good.

CASE 12. J. T., aged 56 years, was admitted to the hospital on July 26, 1950, with a diagnosis of fracture of the neck of the femur. On July 29, an open reduction was performed with Lorenzo screw fixation and there was subsequent nonunion. On March 24, 1951, a second operation was performed with Judet femoral head replacement which subsequently became displaced. These operations were not performed by any of the authors. On October 10, 1951, two of the authors performed a McBride femoral head replacement. During the operation the shaft of the femur inadvertently fractured at the junction of the middle and upper thirds. The patient was treated with balanced traction on a Thomas splint and on February 4, 1952, there was sufficient callus to permit gradual ambulation with the use of a walker. When she was discharged from the hospital, on April 27, 1952, she was ambulatory.

CASE 13. I.M., aged 80 years, was admitted to the hospital on December 13, 1951, and operated on December 15, 1951. The diagnosis was fracture at the base of the neck of the right femur. An open reduction was done with internal fixation with a

Blount plate. Roentgenograms, taken on December 26, 1951, revealed no change in the metallic plate from that seen at the time of operation. A coxa vara deformity remained unchanged. On January 8, 1952, roentgenograms revealed rotation at the fracture site with the blade plate cutting through the neck of the femur. The patient was operated on January 10, 1952, at which time the Blount plate was removed and the head and neck of the fractured femur was replaced by a McBride prosthesis. A cast was applied to the lower leg and the patient's condition postoperatively was fair. The patient responded poorly following operation and a large decubitus ulcer developed over the sacrum. Approximately 1 week following operation the wound exuded old blood and a pressure area developed over the site of the wound. Within a few days the wound was grossly infected showing gram negative bacilli and gram positive cocci by culture. Dakinization was started, and on Feburary 2, 1952 the wound appeared clean and the patient's temperature was normal. However, the patient was aroused with great difficulty and on February 16, 1952, approximately 5 weeks postoperatively, the patient ceased to breathe.

CASE 14. J.C., aged 60 years, was admitted to the hospital on August 19, 1951, operated on September 6, 1951, and discharged on October 22, 1951. The diagnosis was hypertrophic arthritis of both hip joints. Operation consisted of Judet acrylic replacement of the left femoral head. On September 10, 1951, his hip was found to be tight and, on September 26, 1951, traction was applied. On October 6, 1951, the patient was able to get out of bed and was discharged on October 22, 1951, walking on crutches. The patient was examined on January 23, 1952, at which time there was minimal pain about the knee and approximately 20 per cent normal range of motion. The patient was still walking on crutches at that time.

CASE 15. A. R., aged 59 years, was admitted to the hospital on November 14, 1951, operated on December 3, 1951, and discharged on January 5, 1952. The diagnosis was degenerative arthritis of the left hip. The operation consisted of a femoral head replacement with a Judet acrylic prosthesis. A boot cast with board was applied to prevent rotation. When the patient was last seen shortly after discharge from the hospital, there was some residual pain but the patient was moderately comfortable.

CASE 16. T. J., aged 43 years, was admitted to the hospital on November 7, 1951, operated on November 13, 1951, and discharged on December 11, 1951. The diagnosis was ankylosing arthritis of the hips. On November 13, the operation consisted of replacement of the left femoral head with a Judet acrylic prosthesis. The patient was up on crutches on November 30 and was able to bear weight well at the time of his discharge from the hospital. On February 8, 1952, the patient was walking with crutches and stated that his left hip was much improved. There was much improvement in the range of motion of the left hip and the patient felt that his improvement was so great that he desired to have his right hip operated upon also.

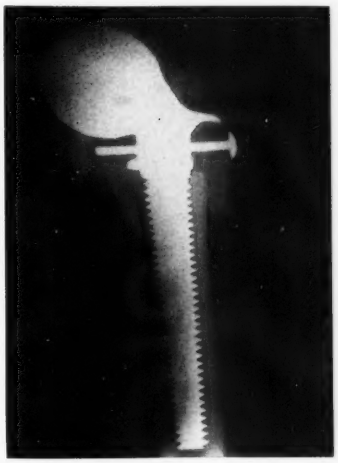

Fig. 1.

CASE 17. F.L., aged 66 years, was admitted to the hospital on July 17, 1951, operated on August 4, 1951, and was discharged on August 31, 1951. The diagnosis was hypertrophic arthritis of the left hip with limited motion. The operation consisted of a Judet replacement with an acrylic prosthetic head. Buck's extension was applied to the left hip on August 15, 1951, and on August 23, the patient was allowed to be up in a wheelchair. At the time of a check-up examination on January 16, 1952, the patient had 20 degrees' flexion deformity, with minimal abduction and rotation. The patient walked with a cane and a slight limp and complained of some discomfort.

Five of these patients (Cases 6, 7, 10, 15, and 16) were not operated upon by the authors but were patients of Dr. Mayer S. DeRoy and Dr. Harry Fisher in the Medical Center Hospitals.

Since this series is small and there has not been an adequate, long term follow-up, it is impossible to offer any conclusions as to final results. Furthermore, many elderly patients die of natural causes or complications of old age and it may, therefore, be impossible to complete many long term follow-ups. Perhaps the value of this study lies in other conclusions that may be drawn. First of all, the same type of prosthesis was not used in all cases nor for the same condition. It will be

Fig. 2.

Fig. 3.

noted that in 3 of the fracture cases the McBride type of prosthesis, which is based on the principle of an intramedullary screw, was found to be relatively easy to insert and very satisfactory for those cases in which there was very little neck or the fracture was trochanteric in location. Our experiences have been only with the acrylic and metallic Judet type of prosthesis which we have found most effective in the transcervical or subcapital types of fractures and the McBride prosthesis, which we have used with satisfaction when the remaining neck is quite short. The material in the McBride prosthesis appears to be nonelectrolytic, and perhaps one of the greatest advantages, which we can see at the moment, is the slight flattened surface of the head which prevents pressure on the cotyloid area of the acetabulum, creating a sort of air pocket which might relieve undue pressure and friction.

It seems to us that the intramedullary application will transmit a more direct weight bearing line into the shaft of the femur and eliminate considerable stress and strain in maintaining weight bearing. A great objection to the McBride head is what has been termed as the loss of bone reserve or bone stock. It is certainly true, as witness in Case 13, I. M., that in case of complication all resources have been lost and, should it be necessary to remove the prosthesis, all that remains is fusion of the proximal portion of the femur to the acetabulum with a marked loss in length. As a corollary with the use of the Judet apparatus, in which an adequate neck remains, should the prosthesis have to be removed, enough bone stock has been preserved to allow for a reconstruction type of operation such as the Whitman procedure (Fig. 1).

The Judet apparatus, whether metallic or acrylic, is particularly easy to insert and is simplicity itself in construction. It has come to our attention that some polymerization has occurred secondary to the use of the acrylics. We personally have had no such experiences and have found no significant difference in the end result between the metallic and acrylic head (Figs. 2, 3, 4, and 5).

What inferences then can we derive from this study of 17 cases so far presented? (1) There was only 1 mortality in these patients of a relatively old age group because of the ability to move them early in bed and get them up quickly with no undue discomfort and thus avoid the many complications that might result from the interruption of normal physiologic function. (2) There need be no fear of the uncertainties of such complications as nonunion or aseptic necrosis. (3) Certainly it is the only method found to date in which one can cease to worry as to whether the patient will bear weight too early. However, there are some disadvantages: (1) A certain amount of bone stock or reserve has to be sacrificed in any of these prostheses. In the Judet type it is minimal. In the McBride it is considerable. (2) With hardly any exception

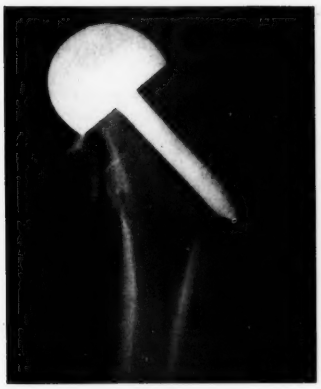

Fig. 4.

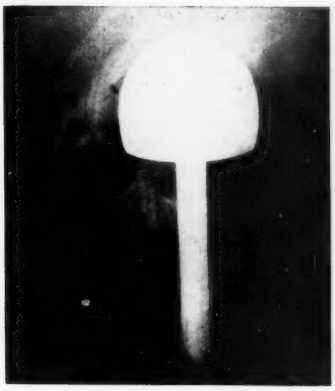

Fig. 5.

these 17 cases has the patient been without some discomfort, limitation of motion, and some limp which, in the long run, is certainly not as satisfactory as the fractured hip which has united primarily and with normal joint surfaces.

It will be noted that in this series the majority of the fractures were of the neck of the femur, 5 of which were acute. Although it is true that no artificial hip can offer the advantages of a normal hip joint, yet we feel justified in advocating the use of the prosthesis in fresh fractures of the neck of the femur encountered in the elderly patient. The reasons we have given before, realizing that there will usually be some residual disability. One of the disabling features is the limp with a positive Trendelenberg sign, which is so frequently seen and persists. It has been suggested that a posterior approach, avoiding the abductor mechanism, might eliminate this difficulty. However, it is difficult to believe that, with an adequate attachment of the trochanteric insertions and the tensor fascia, this should persist with the proper muscle re-education.

A statistical study of these cases reveals that in this series of 17 cases, there has been 1 death and that occurred 5 weeks following operation. The longest follow-up is of 9 months' duration, the shortest of 2 months' duration. Preoperatively we considered Cases 5 and 13 to be the only two carrying a poor prognosis as far as life expectancy was concerned. The oldest patients at the time of surgery were 80, the youngest was 43 years old. The average age was 64 years. The average age of patients with replacements for acute fractures of the neck of the femur was 69. The average age of patients with nonunion was 65. The average age of the arthritics was 57. It is in the younger age group that we will be able to carry out a longer term study, which of course is necessary to evaluate properly the end results of these procedures. It is doubtful whether a clear estimate can be obtained in a follow-up of 5 years and it is hopeful that a few of the younger patients can be followed for at least a 10 year period. There were four complications as follows: (1) hematoma in Case 11 which healed promptly; (2) gross infection of the wound extending down to the prosthesis in Case 13, occurring approximately 1 week after operation and believed to be secondary to contamination of the wound by feces and secondary organisms in a wound which had been complicated by a hematoma. Evacuation was necessary; (3) dislocation of a prosthesis on the eighth postoperative day in Case 5, in which reduction was maintained following closed reduction (This case was one of hemiplegia as a result of an old cerebrovascular accident.); (4) fracture of the shaft of the femur through manipulation at the time of replacement of an unsatisfactory Judet head by a McBride prosthesis in Case 12. We have graded the results to date as follows: 1 excellent, 10 good, 4 fair, and 2 poor.

SUMMARY

In summarizing our experiences with three types of prostheses, we have reached the following conclusions.

1. There appears to be no essential difference in the ultimate result between the acrylic and the metallic type of Judet heads.

2. The Judet appliance has worked quite satisfactorily in those cases in which a sufficiently adequate intact neck was retained.

3. Although for the use of the McBride apparatus it is necessary to sacrifice considerable bone reserve, it has nevertheless worked satisfactorily in those cases without residual neck.

4. The prosthesis is not a completely satisfactory substitute for the normal head and neck, as only 1 of our patients was completely relieved of pain and discomfort and had no limp.

5. We believe, however, that the prosthesis is here to stay, and its use is definitely indicated in the elderly patient whom it is necessary to ambulate early and who cannot be trusted not to bear weight.

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PROPHYLACTIC AND THERAPEUTIC VALUE OF HYDERGINE IN HIGH ALTITUDE FROSTBITE

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WORLD War II is said to have produced a frostbite syndrome which resulted from exposure to extreme degrees of cold at high altitudes. That the syndrome was not completely new is indicated by the fact that Greene, in discussing his experiences in Himalayan expeditions prior to 1940, attributed the loss of a finger tip to the "contact of a momentarily ungloved finger with the button of a camera" at an altitude of about 25,000 feet. It should be noted also that frostbite of aviators did occur during the first World War(21) and during the Spanish Civil War(6), but it was not until the second World War that it became a very definite medical problem. The experiences of the Royal Air Force with this problem have been recorded by Cade and those of the U. S. Army Air Force by Davis, Scarff, Rogers, and Dickinson.

The recent conflict in Korea has already indicated the need for a better understanding of high altitude frostbite and, indeed, of all types of cold injury. The high incidence of cold injury among the United States Army troops participating in the extensive winter combat operations in Korea has been one of the most important medical problems encountered(1). Some workers have, without success, turned to the new "miracle drugs," ACTH and cortisone, in an effort to reduce the extent of injury resulting from experimental frostbite (12, 14).

Extreme vasoconstriction in frostbitten extremities has been noted by several investigators. There is evidence that the sympathetic vasoconstrictor fibers (nonmedullated axons in Remak's fibers) often survive in the presence of inactivation by cold of other fibers in the same nerve bundle. If the thesis is valid that gangrene is the result of anoxia, stasis, and subsequent vascular obliteration, all produced by vasospastic activity, then tissue damage might possibly be prevented by blocking vasoconstriction during the time of exposure to cold. The only damage occurring would then be the result of direct cold injury during freezing and thawing of cells.

With respect to testing this or any other hypothesis, Shumacker and Lempke (18) have remarked that the very circumstance of war which necessitates prompt evacuation of the injured from one medical station to another, making it virtually impossible for one individual to follow any casualty from the time of injury to final rehabilitation, has made it most difficult to study the considerable number of frostbite injuries and to evaluate the therapeutic measures employed. Furthermore, because cold injuries in man vary in severity, duration, and extent of damage, it becomes essentially impossible to obtain a controlled series of investigations. Because of the fact that clinical studies are unsatisfactory, animal experiments have been resorted to by several investigators.

In preliminary studies in this laboratory a mixture of equal parts of three dihydrogenated alkaloids of ergot, namely, dihydroergocornine, dihydroergocristine and dihydroergokryptine, known as hydergine or CCK-179, proved to be of value in the treatment of experimental frostbite (9). This preparation has been found to possess a profound vasodilator effect upon peripheral vessels (16).

METHODS AND MATERIALS

Sixty albino rats of Wistar strain, 90 to 100 days of age and averaging 200 grams in weight, have been used in the present study. A refrigerated decompression chamber was designed with the intent of simulating conditions at which high altitude frostbite occurs (Fig. 1). This decompression chamber consisted of an

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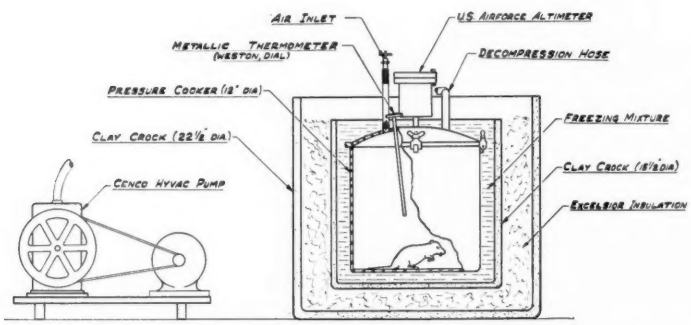

Fig. 1. Refrigerated decompression chamber which was used in these experiments to effect cold injury at a simulated altitude of 25,000 feet.

ordinary pressure cooker, in the lid of which openings were drilled to facilitate installation of an adjustable air inlet, an air outlet, a metallic Weston dial thermometer, and a standard United States Air Force altimeter. The altimeter had been carefully tested by personnel at Lowry Air Force Base in Denver. Decompression was accomplished by a Cenco Hyvac oil vacuum pump of the type found in most chemical laboratories. The entire chamber was fitted into a clay crock which contained a freezing mixture of isopropyl alcohol, ethylene glycol, and solid carbon dioxide. Carbon dioxide was added in sufficient quantity (20 lbs.±) to reduce the temperature of the mixture to −50 degrees C. The chamber was completely submerged in this mixture and the clay crock was in turn set into a larger crock which contained a 7 inch lining of excelsior insulation; thus heat absorption through the sides was adequately prevented. The top of the apparatus was covered by 2 quilted pillows (not seen in Fig. 1) stuffed with excelsior and possessing a thin layer of tin foil on the inner surface; in this manner it was possible to avoid heat absorption through the top.

The rats were placed in the chamber in groups of 5. Decompression was immediately instituted and continued for a period of 5 minutes at which time a simulated altitude of 25,000 feet was reached. Pressure could be maintained within 30 feet of this altitude by adjusting the air inlet valve. The chamber was then lowered into the crock containing the freezing mixture and remained submerged for exactly 15 minutes. A temperature of −40 degrees C. was developed within the chamber in this manner. Decompression began simultaneously with the removal of the chamber from the freezing mixture and required about 3 minutes. After decompression the experimental animals were transferred immediately to cages where frozen tails and limbs were allowed to air-thaw at a temperature of 30 degrees C. (86 degrees F.), maintained by electric light bulbs. The cages were then removed to an air-conditioned animal room.

One group of 20 rats received the dihydrogenated alkaloid preparation prophylactically in 0.5 milligram per kilogram doses administered subcutaneously. Injections were given every 6 hours beginning 24 hours before the time of freezing for a total prophylactic dose of 2.0 milligrams per kilogram of body weight. Following exposure these animals were treated with 0.5 milligram injections given every 3 hours for 24 hours, and then every 6 hours for a minimum of 6 days.

A second group of 10 animals received an oral preparation in identical doses, given at the same intervals per stomach tube. Following cold injury this group received 2.0 milligrams per kilogram of the oral preparation every 12 hours for a total daily dosage of 4.0 milligrams per kilogram of body weight. This schedule was continued for not less than 7 days.

A third group of 10 rats, not treated prophylactically, received the dihydrogenated

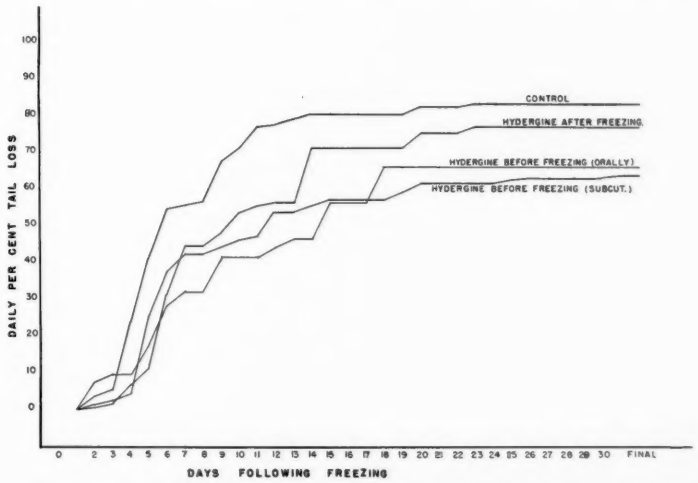

Fig. 2. Graph depicting daily per cent tail loss over a period of 30 days following experimentally produced high altitude frostbite in untreated rats and in rats given hydergine therapeutically or prophylactically.

alkaloids subcutaneously after cold injury. They were given 1.5 milligrams per kilogram immediately after removal from the refrigerated chamber, followed by 0.5 milligram per kilogram every 3 hours for 24 hours and then every 6 hours for 6 days. Finally a fourth group of 20 animals served as controls.

Preliminary investigations have shown that there is a slight variation in the end results from group to group, in spite of every effort to perform each experiment in precisely the same manner. Therefore, control animals were included in each group of 5 rats subjected to simulated high altitude cold.

All animals were observed daily for a period of 30 days. The tails were measured and the per cent daily tail loss due to gangrene was determined (Fig. 2). Final classification of the damage incurred by the hind feet was arrived at somewhat empirically (Fig. 3, Table II) as follows: a tissue-loss value of 5 per cent was given to the phalangeal portion of each toe for a total of 25 per cent if all 5 toes were affected to this extent, 50 per cent to all metatarsals (or 10 per cent loss per metatarsal), and 25 per cent for loss of all tarsal bones. The average differences within each group and between groups of animals, including the controls, were statistically analyzed through the use of Student's "t" test(7).

RESULTS

Upon removal from the chamber, it was found consistently that frostbite had involved the entire tail and both hind feet up to the tibiotarsal joints. These parts appeared waxy, ashen white, ischemic, and shriveled and were found to be frozen solid (Fig. 4, A and B). They accounted for a tapping sound when struck against a wooden table such as is ordinarily produced by a lead pencil. One animal which inadvertently entwined his tail with that of a companion was obliged to wait patiently for the process of thawing to alleviate this situation.

After 10 minutes (in control rats) under an electric bulb in an environmental temperature of 30 degrees C. the affected parts became dark red in color and, though flexible, were quite tense and turgid. Within a half hour the color changed to a deep cyanotic blue, the skin assumed a dull, lusterless appearance and the feet, due to massive edema, assumed the appearance of rubber gloves distended with water (Fig. 4C). The deeper tissues took on a dusky gray hue and eventually became black.

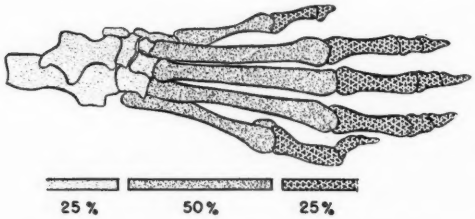

Fig. 3. Diagram indicating per cent values arbitrarily assigned to loss of phalanges, metatarsals, and tarsal bones as the result of experimentally produced frostbite in rats' feet.

The edematous condition persisted for as long as 3 to 7 days in untreated animals, after which the fluid disappeared, the skin became first loose and wrinkled, and then dry, hard, and black. The line of demarcation between black, dry, mummified tissue and pink, soft, viable structure became sharp after 7 to 10 days (Fig. 4E). Spontaneous amputation took place in about 30 to 60 days (Fig. 4G). In most cases, however, the rats gnawed off mummified tissued as it developed. This type of injury would doubtless be classified as fourth degree frostbite by Wright and Allen.

The process described was altered noticeably in those animals which had received prophylactic treatment with hydergine. Though the extent and degree of immediate cold injury were as marked as in the controls (Fig. 4B) thawing under the electric light occurred more rapidly (4 to 6 minutes). Edema and cyanosis developed earlier and were more severe (Fig. 4D) but demarcation and subsequent loss of mummified tissue (Fig. 4F) were delayed, and the eventual tissue loss, due to necrosis, was less (Fig. 4H). These modifications were also seen in the group receiving the dihydrogenated alkaloids therapeutically after freezing but to a lesser degree. It should be mentioned that within the group receiving the dihydrogenated alkaloids prophylactically, a small percentage of animals failed to survive the standard exposure; this may have been due to inability to maintain body temperature in the presence of marked peripheral vasodilation.

The results for all control and experimental groups are summarized in Tables I and II. In Table I the mean per cent tail loss in each group of rats is shown, together with standard error, statistical significance of the differences between each experimental group and the controls, and the statistical data when experimental groups were compared with one another. Mean tail loss in the control animals averaged 84 ± 1.24 per cent. This compared with a loss of 64 ± 4.09 per cent in those rats given prophylactic doses of hydergine subcutaneously. The prophylactic administration of hydergine in the form of an oral preparation was less effective, but the results, on the other hand, were not as variable (67 ± 2.52 per cent).

The least effect with respect to prevention of loss of tail tissue was achieved by administering the dihydrogenated alkaloids subcutaneously after freezing had occurred (77 ± 4.03 per cent). In every case, however, the effect of therapy with hydergine, as arrived at through determination of tail loss, was statistically significant. The oral administration, if intensive, appeared to be quite successful as indicated by the fact that the difference between tissue loss after subcutaneous administration and after oral administration was statistically not significant. Hydergine given before exposure to cold was more effective than its postexposure administration in prevention of subsequent frostbite.

Data from an evaluation of terminal injury as it developed in the hind feet are presented in Table II. A statistically significant difference exists between the mean per cent tissue loss sustained by the control animals and that which ultimately occurred in those animals receiving sympathicolytic therapy. There is also indication of increased benefit from prophylactic, as compared with therapeutic administration of the drug, when hydergine is administered subcutaneously. The results of prophylactic oral administration of hydergine were not significantly different from the results of subcutaneous therapeutic administration after freezing had occurred (Table II).

DISCUSSION

According to Davis and his associates the pathogenesis of frostbite acquired at high altitudes differs in several important respects from that of ordinary frostbite as incurred at lower levels. High altitude frostbite is dis-

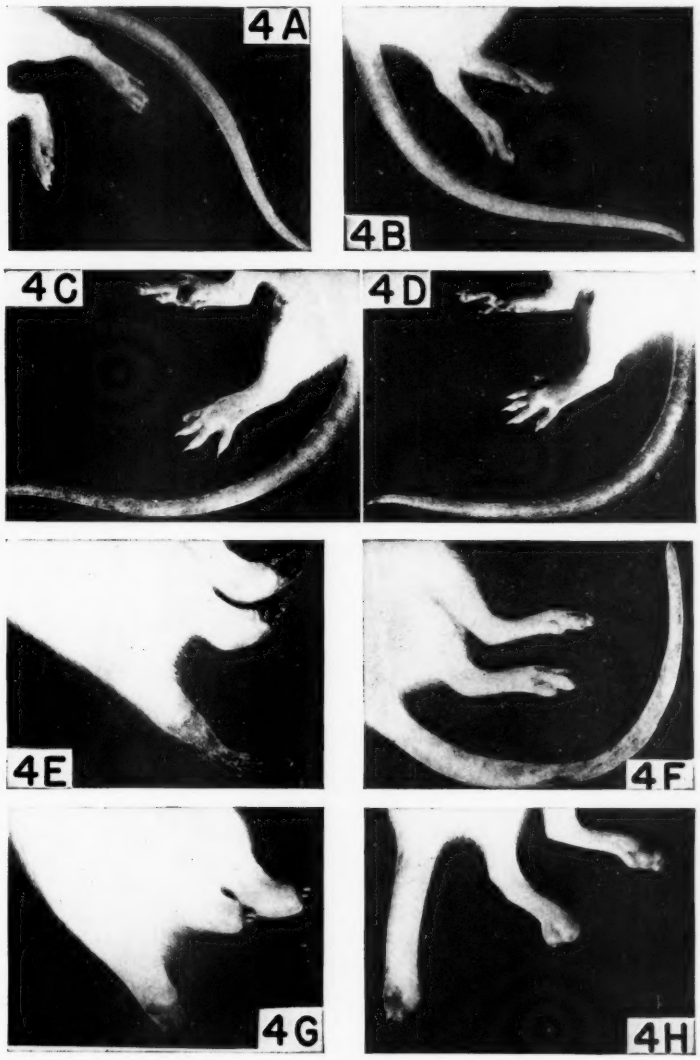

Fig. 4. A, Tail and hind feet of untreated (control) rat immediately after experimental high altitude cold injury. B, Tail and hind feet of rat given prophylactic hydergine as they appeared immediately after high altitude cold injury; this rat and the one shown in A were exposed at the same time to the same environment. C, Tail and hind feet of same animal shown in A as they appeared 30 minutes following high altitude cold injury. D, Tail and hind feet of rat given hydergine prophylactically as they appeared 30 minutes after cold injury; this is the same rat shown in B and C. E, Tail and hind feet of untreated (control) rat shown in A and C as they appeared 14 days after experimental high altitude cold injury. F, Tail and hind feet of prophylactically treated rat shown in B and D as they appeared 14 days after cold injury. G, Tail and hind feet of untreated (control) rat seen in A, C, and E as they appeared 30 days after cold injury. H, Tail and hind feet of prophylactically treated rat shown in B, D, and F as they appeared 30 days after cold injury.

TABLE I.—PERCENTAGE OF TAIL LOSS 30 DAYS AFTER FREEZING

Experimental group	No. in each group	Mean percent tail loss and S.E.m	Difference and S.E.d	$\frac{X_1-X_2}{S.E._d}$	Probability for t of number (n) $[n-(n_1-1)+(n_2-1)]$
Control	20	84±1.24			
Prophylactic hydergine given subcutaneously	20	64±4.09	20±4.27	4.68	<0.001
Prophylactic hydergine given orally	10	67±2.52	17±1.10	15.45	<0.001
Therapeutic hydergine after freezing given subcutaneously	10	77±4.03	7±1.63	4.29	<0.001
Prophylactic hydergine given subcutaneously	20	64±4.09	3±1.86	0.61	<0.500
Prophylactic hydergine given orally	10	67±2.52			
Prophylactic hydergine given subcutaneously	20	64±4.09	13±2.22	5.85	<0.001
Therapeutic hydergine after freezing given subcutaneously	10	77±4.03			
Prophylactic hydergine given orally	10	67±2.52	10±1.84	5.52	<0.001
Therapeutic hydergine after freezing given subcutaneously	10	77±4.03			

tinguished by the extreme cold (−40 to −52 degrees C.) and the presence, not infrequently, of some degree of general anoxia at the time of exposure. The combination of intense cold and anoxemia produces tissue damage in a matter of minutes, whereas, in the case of other types of frostbite, a much longer period of exposure, combined with other factors, such as venous stasis, maceration of tissues, and malnutrition, is necessary for the production of correspondingly severe damage.

It is of particular interest to note, in an airplane at great altitudes, that the face can be exposed for several hours without the occurrence of frostbite but, under similar conditions, the fingers and toes may be so seriously damaged as subsequently to develop gangrene. The explanation of this phenomenon is not clear. Davis and his associates believe that it cannot be explained satisfactorily on the basis of a difference in area of exposed surfaces, since the total radiating surface of the fingers is four or five times as great as that of the cheek. The predilection to frostbite injury manifested by the digits of airmen probably lies in the fact that intense reflex vasospasm of the peripheral arterioles develops and causes ischemia and local anoxia, which is augmented by a pre-existing anoxic anoxia.

A similar predilection was observed in our animal studies. The tails and hind feet were the only parts observed to suffer from the effects of dry cold and decompression while the ears, nose, and other parts of the body were unaffected. The similarity of the capillary structure of the affected parts to that of the extremities of man is well known. We believe that a vasospastic mechanism is a most important factor in the development of tissue injury, for when this mechanism was blocked by the prophylactic administration of hydergine, either orally or subcutaneously, tissue loss was significantly reduced, particularly in the tail, which is especially subject to vasoconstriction.

The inability of some animals receiving the dihydrogenated ergot alkaloids prophylactically to survive our standard exposure was an interesting observation, and prompted some speculation on the pharmacologic effects of these ergot derivatives. Ergotoxine is known to elicit a hypothermic response in rats which are in a cool environment and evidence has been presented in support of the opinion that it acts directly on the thermoregulatory centers of the hypothalamus(2). Stoll and Hofmann(19) isolated 3 primary lysergic acid alkaloids from ergotoxine which have been designated as ergocristine, ergocornine, and ergokryptine. Each of these, when administered singly, has been shown by Rothlin to produce hyperthermia in rabbits. Saturation of the double bond of the lysergic acid portion of the alkaloids by Stoll and Hofmann(20) has produced a new group of so-called dihydrogenated alkaloids of ergot which Rothlin has consistently found to produce hypothermia in rabbits. Roberts and his associates found that dihydroergocristine, dihydroergokryptine, or dihydroergocornine produced hypothermia in

rats; they indicated that the reduction in body temperature was the result of both a peripheral sympathicolytic action and a central hypothalamic depressive action. It therefore seems reasonable that the animals receiving prophylactic hydergine (which is a combination of the 3 hydrogenated alkaloids investigated by Roberts *et al.*) should demonstrate a reduced tolerance to cold. Vasoconstriction, which is in the beginning a natural diffuse mechanism of the body, was apparently prevented with resultant loss of body heat. A related phenomenon has been described by Heppert and others who found that the rise in blood pressure in the cold pressor test may be diminished by hydergine. It is important to note, however, that most animals subjected to experimental high altitude cold are able to adjust their metabolic processes to the increased stress, and as a result, are able to survive the procedure.

The present literature indicates that damage due to freezing of tissues is the result of two factors: first, the direct effect of cold upon the cells during freezing and thawing; and second, the indirect effect of ischemia, anoxia, and consequent increased permeability of the capillary membrane, edema, and agglutinative thrombosis, all of which follow vasoconstriction. We believe that the latter is of utmost importance in the pathogenesis of high altitude frostbite as produced in our experimental animals. Contrary to the opinion of Lake freezing per se does not consistently injure cells. All who have studied experimental frostbite have seen tissues, seemingly dead, gradually return to life and regain their function. Burdenko considered frostbite to be a "syndrome which consists of a disturbance of blood circulation through a reflex spasm of the capillaries and arterioles, and a disturbance of nutrition due to damage of the neurotropic apparatus." Shumacker and Lempke(18) and Lempke and Shumacker(12) have conclusively demonstrated that rapid thawing is of very real value in the treatment of cold injury, and Shumacker(17) has also recently concluded that "sympathectomy has a definite place in the management of cryopathies." The benefit derived from both of these procedures is due largely to the release of blood vessels from vasoconstrictive nerve impulses.

TABLE II.—PERCENTAGE OF LOSS OF HIND FEET 30 DAYS AFTER FREEZING

Experimental group	No. in each group	Mean percent hind feet loss and S.E.$_m$	Difference and S.E.$_d$	$\frac{-t-X_1-X_2}{S.E._d}$	Probability for t of number n $[n-(n_1)+(n_2-1)]$
Control	20	37.29±9.51			
Prophylactic hydergine given subcutaneously	20	9.67±3.67	27.62±3.38	8.17	>0.001
Prophylactic hydergine given orally	10	18.50±4.98	18.79±4.16	4.51	<0.001
Therapeutic hydergine after freezing given subcutaneously	10	19.13±4.37	18.16±4.05	4.47	<0.001
Prophylactic hydergine given subcutaneously	20	9.67±3.67	8.83±2.38	3.71	<0.001
Prophylactic hydergine given orally	10	18.50±4.98			
Prophylactic hydergine given subcutaneously	20	9.67±3.67	9.46±2.20	4.30	<0.001
Therapeutic hydergine after freezing given subcutaneously	10	19.13±4.37			
Prophylactic hydergine given orally	10	18.50±4.98	0.63±2.56	0.246	<0.800
Therapeutic hydergine after freezing given subcutaneously	10	19.13±4.37			

On the basis of the experiments reported herein and as indicated by the observations of others (5, 13, 17) optimum therapeutic results in human frostbite can be anticipated if therapy is instituted while the airman is still in flight, or when the foot soldier first appears at an aid station. Nerve blocking procedures, which require exacting surgical skill, are completely impractical at these critical points in the course of the frostbite. High altitude frostbite is a medical problem which should be considered a vascular emergency, as certainly as is sudden arterial occlusion. Its recognition and immediate treatment are of utmost importance and present a challenge to every military physician.

SUMMARY

World War II served to emphasize the seriousness of a unique frostbite syndrome which resulted from exposure to extreme degrees of cold at high altitudes. High altitude frostbite is distinguished by extreme cold and the presence of some degree of anoxic anoxia at the time of exposure; consequently, it is not a pure example of tissue injury due to cold. If high altitude frostbite can be considered as a syndrome resulting from intense vasospastic activity, then tissue damage should be prevented by blocking this reflex during exposure to cold.

In this study, hydergine, a combination of dihydrogenated ergot alkaloids and an effective adrenergic blocking agent, was administered prophylactically to 30 white rats of Wistar strain before exposure to a standard cold injury under conditions simulating an altitude of 25,000 feet. Twenty animals received the drug subcutaneously and 10 animals were given an oral preparation by means of a stomach tube. Another group of 10 was treated with hydergine subcutaneously after freezing and a last group of 20 animals served as controls. The therapeutic results in each treated group, when compared with the end results in untreated controls, were statistically significant. The mean per cent tail loss in the groups receiving either oral or subcutaneous hydergine prophylactically was significantly less than the mean per cent tail loss sustained by the group receiving the dihydrogenated alkaloids after freezing. Optimum results can be anticipated if therapy is instituted early or before thrombosis has taken place.

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COMMON DUCT EXPLORATION FOR STONES

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EXPLORATION of the common bile duct and its tributaries for stones is a surgical procedure of 60 years' standing. One of the first to report its successful accomplishment was Kümmel in 1890. It is commonly employed today by all surgical services that treat biliary tract disease, but the frequency of its use varies greatly from one clinic to another. Some explore the common duct for stones only in the presence of certain indications, whereas others carry out choledochotomy almost routinely in conjunction with cholecystectomy for cholelithiasis.

Because such wide variation is found in the reported series, both as to the frequency of exploration and the incidence of stones recovered, a study has been made of the experience on the surgical pavilions of the New York Hospital-Cornell Medical Center over an 18 year period. A brief review of this clinical experience is presented and compared with that of several other representative clinics throughout the country. The indications for exploring the common duct are given, together with methods and results. The progress that has been achieved in biliary tract surgery is emphasized in this study, but the hazards that continue to exist should not be underestimated. Finally it is suggested that the importance of early interruption of biliary tract disease lies in its probable prevention of complications and sequelae, such as choledocholithiasis, biliary cirrhosis, liver damage, and carcinoma of the liver or bile ducts.

During the 18 year period from 1932 to 1950, 3,439 patients on the surgical pavilions of the New York Hospital-Cornell Medical Center were operated upon for nonmalignant disease of the biliary tract. Of this number, 421 patients were also subjected to choledochotomy in search of stones presumed to be present on the basis of certain criteria. For 62 patients of this group, choledochotomy was a secondary procedure, cholecystectomy with or without choledochotomy having been done previously (Table I).

We explore the common duct for stones in combination with cholecystectomy for cholelithiasis under the following conditions: (1) palpable stone within the common duct; (2) a history of jaundice preceded by or associated with pain or intermittent elevation of temperature; (3) a thickened common duct wall, with or without dilatation (This should be distinguished from edema of the common duct found in acute and subacute inflammation of the gallbladder and associated with a mild degree of jaundice, namely an icteric index of 30 or less.); (4) contracted gallbladder containing stones; (5) dilated cystic duct; (6) enlarged head of the pancreas (This may be due to inflammation associated with stones in the lower end of the common duct or in the ampulla of Vater, but it may be due to malignant disease. One should determine at operation whether the history, recent clinical course, and findings favor stones, pancreatitis, or cancer, and proceed accordingly.); (7) if the patient is over 60 years old and has a prolonged history of biliary tract disease.

METHOD

If common duct exploration is to be done at the time of a cholecystectomy, the gallbladder will serve a purpose if it is removed downward from its fundus. The cystic artery and the cystic duct are first identified and secured and the gallbladder then dissected from its bed in the liver. The cystic duct is left intact with a ligature about it just distal to the ampulla of the gallbladder to prevent small stones from passing through the cystic duct into the common duct. An incision may then be made in the cystic duct and a small catheter introduced into the common duct. If desired, cholangiograms may be done at this time by introducing opaque material into the common duct by way of the catheter in the cystic duct.

To explore the common duct, a linear incision is made in the anterior wall of the duct, 2

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Fig. 1. If common duct exploration is to be done at the time of a cholecystectomy, the gallbladder will serve a purpose if it is removed downward from the fundus. The cystic artery and the cystic duct are first identified and secured, and the gallbladder then is dissected from its bed in the liver. The cystic duct is left intact with a ligature about it just distal to the ampulla of the gallbladder to prevent small stones from passing through the cystic duct into the common duct. After exploration of the common duct, if for any reason a free passage into the duodenum cannot be demonstrated, then transduodenal exposure of the ampulla through a longitudinal incision should follow.

centimeters in length and extending from just above where the duct passes beneath or into the substance of the pancreas. Two traction sutures of fine silk are used to hold the walls of the duct apart. As bile escapes, it is removed by suction. In many cases, stones are carried out of the duct with the escaping bile. A few minutes' observation without molesting the operative field may see additional stones brought from the more remote sections of the biliary tract by the bile. Indeed, the flow of bile is an important aid in removing these stones which may so easily become impacted in the smaller tributaries as one attempts to explore for them mechanically. After decompressing the biliary tract and removing such stones as have appeared in this aperture, the distal portion of the common duct is explored by flushing saline through a soft catheter and then using a malleable pituitary spoon. Most stones are encountered in the region of the ampulla of Vater. When found, every effort should be made to remove them intact, but if they are fragmented, precaution should be taken to remove all the fragments. After exploring that portion of the duct distal to the opening with the pituitary spoon, the proximal section is explored. A rubber catheter or woven silk bougie is then used to demonstrate the passageway into the duodenum. The catheter may be passed into the duodenum easily even though a stone may be impacted in the ampulla. A soft malleable probe is often helpful to demonstrate a stone in this particular region. These three aids are then in turn used again to explore the proximal tributaries. Gentle irrigation of the tributaries with the catheter may often dislodge stones, but it can sometimes cause further impaction. Therefore caution should be exercised as to the pressure used in irrigating the tributaries.

After a thorough exploration and the removal of such stones as may have been encountered, cholangiograms are repeated. A small catheter is inserted through the cystic duct into the common duct and the common duct is closed with a continuous suture and occluded by means of a rubber-shod clamp placed as near the pancreas as possible. Twenty cubic centimeters of 50 per cent diodrast are then introduced into the extrahepatic system through the catheter, and a picture is taken immediately. The rubber clamp is then removed and another picture taken 5 minutes after the first. These are both developed immediately and examined. If they show obstruction in the region of the ampulla of Vater or in the distal portion of the common duct, a third picture is taken 10 minutes after the second. If stones are revealed they are removed and the cholangiograms repeated.

On completion of the exploration, the gallbladder is removed, a half centimeter stump of cystic duct is left distal to its junction with the common duct, and the catheter within it is secured by a transfixing suture of No. 000 chromic catgut. The tip of the catheter is allowed to extend just beyond the distal extremity of the linear incision in the common duct. The incision is then repaired with a series of interrupted sutures of No. 000 plain catgut, inverting the serosa, and is reinforced with a series of interrupted sutures of fine silk.

The methods and the aids employed to attain the objective of removing all possible stones are numerous and ingenious. Perhaps no two surgeons use the same technique or the same tools. Each seeks to develop his own routine that will best enable him to remove all the stones and leave none behind. Catheters, bougies, probes, intraductal lighting, and the cholelithophone devised by Kirby and Thurston are all aids whose value is more dependent upon the skill of the surgeon who uses them than on their nature or construction. Cholangiograms consistently reveal stones that might otherwise be overlooked, but they are not infallible. Frequently stones become apparent after operation which were undoubtedly present prior to exploration. There are certain refinements in taking cholangiograms that will contribute to their success. The head of the table should always be lowered before the diodrast is introduced and the dye should be injected slowly and at a constant pressure over a period of 2 or 3 minutes with the distal portion of the common duct occluded. Undue pressure should never be exerted when injecting this material. After the pictures are taken, the diodrast should be removed and the biliary tract flushed with saline. While the biliary tract is decompressed and without molesting the operative field, stones will often float through the aperture with the bile. When doing cholangiograms, much time can be saved by having everything ready at the operating table and by having complete co-operation from those who take and develop the pictures.

When common duct exploration and cholangiography are done on patients who have already had the gallbladder removed, the same method is used. A large needle attached to a 30 cubic centimeter syringe is used to inject the diodrast either before exploration or after with the incision closed. In all secondary operations on the common duct a T tube is used for drainage. When the T tube is used, care should be exercised to make sure that the proximal limb does not extend beyond the bifurcation of the common duct into one of the main tributaries, or protrude down into the ampulla of Vater, except on rare occasions.

TABLE 1.—CHOLEDOCHOTOMY FOR PRESUMED COMMON DUCT STONES IN 3,439 PATIENTS WITH NONMALIGNANT DISEASE OF THE BILIARY TRACT

New York Hospital,
September 1, 1932 to September 1, 1950

		Choledochotomy findings		
	No. of cases	Stones recovered	No stones recovered	Deaths
Acute cholecystitis.....	67	41	26	3
Chronic cholecystitis.....	292	193	99	17
	359	234	125	20
Previous cholecystectomy with or without choledochotomy.....	62	42	20	4
Totals.....	421	276	145	24

In our experience, the most common site for an overlooked stone is just proximal to the ampulla of Vater. Introduction of a catheter, bougie, or probe through the lower bile duct into the duodenum, with careful palpation along its course from both right and left sides of the patient, will often reveal stones that would otherwise be overlooked. When for any reason a free passage into the duodenum cannot be demonstrated, then transduodenal exposure of the ampulla of Vater should follow. The ampulla can be palpated with ease and then secured with fine silk sutures in the duodenal wall just adjacent to it. A pliable small woven silk bougie can then be introduced into the ampulla and passed up into the common duct, followed by a soft rubber catheter of slightly greater diameter. Palpating along the course of the catheter, the operator can accurately locate the stone. Thereafter, with the aid of forceps or a small pituitary spoon, the stone may be removed through the common duct itself or the ampulla below. The ampulla may be dilated gradually to facilitate this procedure. Except in unusual circumstances we prefer not to transect the sphincter of Oddi.

In all patients who have been subjected to common duct exploration cholangiograms are repeated about 10 days after operation unless there is a contraindication. These films are taken in the x-ray department on a tilting table, with the head of the table lowered approximately 15 degrees, and the diodrast is allowed to flow into the common duct drainage tube by a gravity of less than 10 to 20 centimeters of water. The picture is taken as the last of the dye enters the system.

TABLE II.—REPORTED INCIDENCE AND RESULTS OF COMMON DUCT EXPLORATION COMBINED WITH CHOLECYSTECTOMY

		Exploration		Stones recovered		
	No. of cases	No.	Per cent	No. cases	Per cent of expl.	Per cent of total
Lahey 1910–1926....	619	96	15.5	52	54.0	8.4
1927–1931....	653	211	32.4	88	41.0	14.0
Cattell 1930–1933....	493	198	40.2	98	49.8	20.0
1934–1937....	634	284	44.8	103	36.0	16.2
1938–1941....	909	444	48.8	128	28.9	14.1
1942–1945....	1,104	504	45.7	186	36.7	16.8
Walters 1946.....	1,259	301	24.0	—	50.0	12.0
McKittrick and Wilson 1949.....	100	100	100.0	52	52.0	52.0
McLaughlin and Kleager 1950.....	230	71	30.7	—	33.8	10.0
Glenn 1932–1938....	895	100	11.2	55	55.0	6.2
1939–1950....	2,472	259	10.5	179	69.1	7.2

If stones are demonstrated after operation, usually they should be removed. Cholangiograms should be repeated if stones are thought to exist, since an erroneous conclusion may be reached from visualizing a defect that is the result of diodrast displaced by an air bubble or by concentrated bile. If the stones are half a centimeter or more in diameter, we believe that operation should be undertaken before the tube in the common duct is removed. With smaller stones, removal of the tube and observation of the patients are indicated, as these stones may often be passed. On the other hand, they may not pass and may increase in size. Certainly such patients as are under observation should be subjected to operation if they develop signs of obstruction.

We have abandoned completely any attempt to remove stones by the method described by Pribram. Severe reaction has been observed immediately afterward as well as delayed cholangitis following the use of the solvents he advocates, or their variations. Within a period of 48 hours we have observed what was believed to be a cholangitis manifested by right upper quadrant pain and discomfort, anorexia, nausea, elevation of temperature, and an increase in leucocytosis as well as varying degrees of jaundice.

COMPARATIVE EXPERIENCE

A review of the literature on this subject would lead one to assume that there is general agreement as to the indications for exploring the common duct. In fact, many authors list the same criteria. However, a wide difference is found in the frequency with which the duct is opened in quest of stones and in the incidence of calculi recovered. By and large, those who report the greatest proportion of explorations also report the highest incidence of stones recovered. Table II tends to lend emphasis to this statement. McKittrick and Wilson, for example, report 100 choledochotomies combined routinely with cholecystectomy for cholelithiasis and show recovery of stones in the common duct in 52 per cent of their cases. The other extreme is our own experience at the New York Hospital-Cornell Medical Center. Of the 3,367 patients subjected to either cholecystectomy or cholecystostomy, choledochotomy in search of stones was done as well in only 359 cases, or 10.6 per cent. Stones, however, were recovered in 65 per cent of those explored, or 6.9 per cent of the total series. In an earlier report from our clinic (1938)(2) of 895 patients subjected to cholecystectomy or cholecystostomy, choledochotomy was done in 100, or 11.2 per cent. Stones were recovered in 55 cases, 55 per cent of those explored, 6.2 per cent of the total series of 895 cases.

It is evident that there is considerable variation in the experience of the surgeons who explore the common duct. Part of the difference may lie in the fact that when a gallbladder is manipulated at operation, small stones may pass through the cystic duct into the common duct and are then found when the duct is opened. Finding small stones under these circumstances, however, does not necessarily indicate that common duct obstruction will result from them. It should also be mentioned that stones may exist in the common duct and yet not produce symptoms. However, the fact that a patient is without symptoms of common duct stones following cholecystectomy does not rule out their possible presence. If stones in the common duct are looked upon as a complication or sequela of gallstones, then it follows that the longer cholelithiasis has been present the greater is the likelihood of choledocholithiasis. The older the patient is and the longer the disease has existed, the greater may be the expected incidence of

common duct stones. If all age groups are included and allowance is made for silent common duct stones, not omitting the findings from autopsy studies, it is our opinion that the true incidence of retained common duct stones is about 10 per cent. In other words, of all patients with stones in the gallbladder, 1 in 10 will also have stones in the common duct.

It was of interest to us to determine whether the incidence of stones recovered was greater in patients who underwent choledochotomy after the age of 50 than in those under 50 years old (Table III).

It was noted that a slightly higher incidence of stones was found in the older patients than in the younger group, 67.1 to 63.9 per cent, but more significant was the difference in the mortality rate. For the older group it was 9.6 per cent, whereas for the younger patients it was only 1.5 per cent.

On reviewing the reports from other clinics (Table II), we became concerned as to whether we were exploring the common duct at the time of cholecystectomy often enough. To evaluate our policy, a careful follow-up study was made on 100 patients who had undergone a cholecystectomy without common duct exploration. These patients had been followed for 10 years or more and were selected irrespective of age, sex, or history. According to our criteria, choledochotomy was not indicated at the time of their cholecystectomy. The results of this study were as follows: no signs or symptoms of common duct stones were present in 93 cases; symptoms leading to common duct exploration developed in 7 cases; stones were recovered in 4 cases; and no stones were found in 3 cases. These results are not entirely satisfactory, but no comparable studies were found in the reports of those who explore the common duct more frequently. However, since these stones were present at the time cholecystectomy was done and they might have been removed then, we are prompted to scrutinize our patients even more carefully, and if there is any question as to the presence of a stone exploration is carried out. Of equal concern have been those patients in whom common duct exploration combined with cholecystectomy has been performed. To evaluate our results with this group, we studied 100 patients in whom both procedures were done at one operation 3 to 18 years ago (Table IV).

TABLE III.—CHOLEDOCHOTOMY BY AGE GROUPS

New York Hospital, 1932 to 1950

Operative findings	Patients under 50	Patients over 50	Total cases
Stones recovered	129	147	276
No stones found	73	72	145
	202	219	421
Operative mortality			
Stones recovered	3	16	19
No stones found	–	5	5
	3	21	24
Mortality rate, per cent	1.5	9.6	5.7

It must be expected that some of the patients upon whom a cholecystectomy was performed at our clinic might develop signs and symptoms of common duct stones at some later time and undergo choledochotomy at another hospital, since patients have come to us for a secondary operation following cholecystectomy done elsewhere. For this reason, our reported incidence of stones overlooked may be lower than it should be.

In our series of 421 patients subjected to common duct exploration from the total series of 3,439 patients operated on for nonmalignant disease of the biliary tract, there were 24 deaths, a mortality of 5.7 per cent for choledochotomy. This is a great improvement over reports issued prior to 1932. More significant, however, is the steady drop in the mortality rate since 1932. The first 100 choledochotomies of our group were reported in 1938 with a mortality of 10 per cent. Since then the balance of 321 patients were operated on with a mortality of 14, or only 4.36 per cent for the last 12 years.

A review of the tabular analysis of these 24 deaths (Table V) shows that hemorrhage and infection, the chief causes of death in the early years of our experience, have become well controlled. Deaths attributed to liver impairment, however, continue to occur in about the same proportion and accounted for 10 of the 24 deaths. Liver damage is difficult to recognize and to evaluate, and thus is often overlooked. For the most part, it is found among the patients with a long history of biliary

TABLE IV.—100 PATIENTS SUBJECTED TO COMMON DUCT EXPLORATION COMBINED WITH CHOLECYSTECTOMY

New York Hospital, 1932 to 1950
3 to 18 years follow-up

	No. cases	Incidence per cent
Common duct stones recovered on exploration.	54	
Recurrence of symptoms leading to re-exploration	6	
Stones recovered at re-exploration	5	9.7
No stones found at primary exploration	46	
Stones recovered on subsequent re-exploration.	2	4.2

tract disease. Cardiovascular disease in its various forms, ranging from a moderate degree of arteriosclerosis to a fulminating hypertension, has become a frequent cause of death in recent years. This is to be expected, since more elderly patients are now subjected to operation than formerly, but the overall trend of the mortality rate and morbidity of complications is quite encouraging.

DISCUSSION

During the years from 1890 to 1920 the mortality rate associated with choledochotomy was very high. The procedure was, therefore, often delayed but finally done in desperation. From 1920 to 1935, as with many other procedures, exploration of the common duct became an established operation, to be undertaken when indicated. Although the mortality rate had fallen decidedly, there was still considerable hazard associated with the procedure because of the bleeding tendency common in jaundice and uncontrolled infection. Since 1935, the mortality rate has fallen even further, as has the morbidity from complications, even though the procedure is now done more often on older and on severely ill patients. The most important contribution to this trend in recent years has been the introduction of vitamin K which has almost completely removed the hazard of hemorrhage. This was formerly a common cause of death in the jaundiced patient. Then chemotherapy was introduced, first in the form of the sulfonamides and later the antibiotics, enabling us to control infection to a remarkable degree both within the biliary tract and in the operative area. These could be said to run a close second in importance. They, together with other general advancements, such as better anesthesia and better understanding of water, electrolyte, and nutritional requirements, have helped reduce the risk of surgical procedures on the biliary tract to a figure commensurate with operations of lesser magnitude. The statistics presented herein correspond with those shown in other recent papers which fact indicates that common duct exploration is a far less hazardous procedure than it was 20 years ago.

In any discussion of stones in the common duct, particular attention should be given to those patients with jaundice before operation is embarked upon. It is important to know whether there is liver damage, and if so, its extent. If extensive, the administration of an anesthetic agent that is toxic or that deprives the liver of sufficient oxygen may render the anesthesia incompatible with life. Yet the liver is known to have a remarkable capacity for repair and even regeneration, so that if such a patient receives the necessary nutritional elements and rest, liver repair may take place quite rapidly. On the other hand, mere waiting may also be associated with further liver damage. Therefore, from a practical standpoint, all jaundiced patients merit particularly careful evaluation as quickly as possible. If it is decided that liver function and reserve are good, then operation should not be postponed, but should be carried out with the precautions that will protect the liver. When liver function is impaired, every step known to contribute to its improvement should be taken, and operation should be undertaken when correction has reached its maximum. The least toxic anesthetic agent should be used together with a high oxygen supply, and the operation should be limited in scope to an objective within the patient's capacity. It may be necessary to confine it to simple decompression of a completely obstructed common duct without removing the cause of obstruction. This may have to be postponed until a later date in order to allow some liver repair to take place first.

The clinical picture of cholecystitis and cholelithiasis is well known to the profession because of its frequency and because of its

TABLE V.—ANALYSIS OF 24 DEATHS FOLLOWING EXPLORATION OF THE COMMON BILE DUCT

New York Hospital, 1932 to 1950

History number	Sex	Age	Jaundice	Operation	Stones in common duct	Cause of death	Autopsy
33-617	M	62	Yes	Cholecystectomy, choledochotomy	2 at oper., 1 at autopsy	Subphrenic abscess; biliary cirrhosis	Yes
159-038	M	57	Yes	Cholecystectomy, choledochotomy	2	Hemorrhage; erosion of portal vein	Yes
144-052	M	53	Yes	Cholecystectomy, choledochotomy	Cast	Bronchopneumonia; pulmonary embolism	No
7-460	M	44	Yes	Cholecystectomy, choledochotomy	16 impacted	Biliary cirrhosis; hemorrhage	Yes
46-479	F	33	Yes	Cholecystectomy, choledochotomy	Stones in ampulla	Hemorrhage; pulmonary edema	Yes
164-530	M	50	Yes	Cholecystectomy, choledochotomy	No	Bronchopneumonia; shock	No
60-269	M	52	Yes	Cholecystectomy, choledochotomy	Yes	Biliary stenosis; shock; cirrhosis	No
80-467	M	54	Yes	*Cholecystectomy, choledochotomy	9	Hemorrhage; choleduodenocolic fistula	Yes
92-066	M	54	Yes	Cholecystectomy, choledochotomy	1 in liver	Necrosis urinary bladder; hepatic abscesses	Yes
202-305	F	76	Yes	*Excision of fistula; choledochotomy	Yes	Cholangitis; central necrosis of liver	Yes
230-507	F	59	No	Cholecystectomy, choledochotomy	2	Peritonitis; perforation of diverticulitis	Yes
207-505	F	50	No	Cholecystectomy, choledochotomy	Several	Pulmonary embolus	No
318-938	M	69	Yes	Cholecystectomy, choledochotomy	No	Peritonitis; c.d. & duodenal leakage	Yes
344-681	M	59	Yes	Cholecystectomy, choledochotomy	Yes	Bronchopneumonia 26th p.o. day	No
365-980	F	64	Slight	Cholecystectomy, choledochotomy	1	General peritonitis	Yes
36-604	F	62	Yes	*Choledochotomy, duodenotomy	1	Anuria; uremia	No
304-576	F	54	Yes	Cholecystectomy, choledochotomy	2	Subdiaphragmatic abscess	Yes
403-583	F	67	Yes	Secondary choledochotomy	1 found at autopsy	Stone in common duct	Yes
411-366	M	60	Yes	Cholecystectomy, choledochotomy	Yes	Stone left in c.d.; bronchopneumonia	Yes
105-722	M	56	Yes	Cholecystectomy, choledochotomy	Stenosis only	Myocardial infarction 26th p.o. day	No
444-268	M	67	No	Cholecystectomy, choledochotomy	Many	Congestive heart failure	No
445-259	M	39	No	Cholecystectomy, choledochotomy	Yes	Renal failure, biliary fistula, fecal fistula	Yes
536-825	M	71	Yes	Cholecystectomy, choledochotomy	Yes	Coronary occlusion	Yes
573-261	F	81	Yes	Secondary choledochotomy	No	Laennec's cirrhosis, hepatic failure	Yes

*Secondary to cholecystectomy.

widely reported management. Diagnosis may be easily confirmed by cholecystography and by examination of the duodenal contents. Many of these patients are guided by diet regulation and other medical measures that encourage them to tolerate the disease. Others are treated promptly by surgical removal of the gallbladder containing stones. There is considerable evidence to show that the latter is the most effective method of interrupting the progress of the disease. If operation is carried out early, before the common sequelae and complications can develop, it is likely that they will be prevented. The risk of cholecystectomy for cholelithiasis is low. The mortality for all ages is about 0.5 per cent. For patients in the younger age group the risk is even less. Cholecystitis with cholelithiasis often appears in early adult life, especially among women after the first or second pregnancy. If surgery is carried out early in the course of cholelithiasis, it should surely reduce the incidence of stones in the common duct. Stones in the common duct are rarely found in patients who have no stones in the gallbladder. Prophylactic measures to prevent the formation of biliary calculi are as yet lacking, but it is believed that their incidence is higher in those who indulge in a high cholesterol diet and in women who have been pregnant. It is hoped that preventive measures will be developed, but until they are, early surgical intervention is indicated.

Those who operate on the biliary tract should be prepared to undertake common duct exploration on any patient undergoing chole-

cystectomy. Even though the history lacks definite indication for opening the common duct, the final decision should not be reached until a careful examination of the extrahepatic biliary system and the pancreas has been made. If the surgeon is not satisfied with his search for intraductal stones through an incision in the common duct and he feels that one may be concealed in the lower portion of the ampulla of Vater, then a transduodenal approach to explore that area is indicated. If difficulty is encountered in passing the exploring instruments into the duodenum from above, it is far safer to expose the ampulla and catheterize it under direct vision. The old objection that such a procedure would lead to duodenal fistula is no longer valid if the intestine is properly closed.

Common duct exploration is accomplished today with a lower mortality and morbidity than ever before, but it is a procedure that requires time, care, and skill to perform successfully. It should be done preferably only under certain circumstances. Once the decision to explore the common duct is reached, it should be carried out in a well planned and thorough manner. At the end of the operation the surgeon should feel that he has left nothing undone that would help locate and remove any stones that might be present. If choledochotomy is carried out with the belief that stones are present, the search will usually be more successful than if done as a routine procedure.

CONCLUSIONS

Common duct stones may be considered a complication or sequela of cholelithiasis. Their incidence increases with the duration of biliary tract disease and may be expected more frequently in the older age group. The early surgical interruption of biliary tract disease, while stones are limited to the gallbladder only, is perhaps the best prophylactic measure available to prevent the formation of common duct stones. The most effective means of determining their presence and achieving their removal is by common duct exploration. In general, when indicated, such exploration should be undertaken at the time cholecystectomy is done for cholelithiasis, but it should not be regarded as a routine procedure. It is an operation that should be done only by those who are equipped and prepared to do it with care and thoroughness.

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RELATIONSHIP OF POSTCHOLECYSTECTOMY DISTURBANCES TO BACTERIAL SENSITIVITY

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THE postcholecystectomy syndrome remains an unsolved surgical problem. In a group of 119 cholecystectomies Bettman and Lichtenstein reported 18 per cent unsatisfactory results when stones were present and 33 per cent failures when the cholecystic disease was not associated with calculi. Weir and Snell state that good results are obtained in 88 to 90 per cent of the cases in which stones are present. The end results were much more favorable in the "follow-up" study of Eliason and North who found residual symptoms after 1 year in only 6 per cent of a group of 264 patients in whom cholecystectomy had been performed. Few surgeons have been able to match this record and in the present investigation disappointing results were reported by 28 per cent of 149 patients followed 6 months to 3 years. A further analysis indicated that 26 per cent of the cholelithiasis group resulted in failures while among the noncalculous patients the incidence of unsatisfactory results was 45 per cent.

Numerous hypotheses have been advanced to explain this distressing syndrome but none satisfies all situations. Residual stones in the hepatic ducts, dilatation of the cystic duct stump, and pancreatic duct obstruction are known to account for a small percentage of the failures; reference frequently is made to biliary dyskinesia as an explanation for others. Weir and Snell assert that associated lesions of the liver and pancreas occur in as many as 20 per cent of patients with cholecystic disease and believe they may explain many residual complications. Pribram's recent excellent paper on postcholecystectomy syndromes suggests that the persistence of acute and subacute symptoms referable to the biliary and alimentary tracts after cholecystectomy may be due to several causes which he classifies as follows: "(1) the pressure syndromes due to the missing tension bulb function of the gallbladder and their secondary complications, cholangiohepatitis and pancreatitis; (2) the lowered tolerance for food, especially fatty food, due to the missing digestive aid of concentrated gallbladder bile and the hormone secreted from the wall of the gallbladder; (3) paralysis of the sphincter, leading to diarrhea and enteritis."

The literature contains numerous references to the probable relationship between gastrointestinal allergy and biliary colic. This hypothesis was first proposed by Singer who believed that sensitivity to egg albumen is frequently responsible for subjective symptoms resembling gallbladder colic. He called attention to the hepatomegaly observed in experimental animals following inoculation with peptone or histamine and held the opinion that a similar condition may occur in humans who are sensitive to albumen. In 1928 Graham in his monograph, *Diseases of the Gall Bladder*, suggested that serious consideration be given intestinal allergy as an etiologic factor in chronic cholecystitis. Deissler and Higgins studied the behavior of gallbladders of guinea pigs sensitized to horse serum when subjected to additional stimulation with the antigen. They observed that the resulting contractions of the gallbladder raised the pressure within the organ to a much higher level than that at which rhythmic activity was observed; moreover, the resistance of the sphincteric mechanism of the ductus choledochus during maximal stimulation was found to be greater than the maximal pressure of the gallbladder; when the gallbladder contracted it failed to empty. In discussing these results Alvarez reported several cases typical of chronic cholecystitis and biliary colic in which normal gallbladders were found at operation and in each of which

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dramatic improvement was observed following an elimination diet. The following year Rehfuss referred to the frequent association of allergic conditions and biliary tract disease. More recently Muro and Ficari have published the results of an interesting study of the histologic findings in gallbladders of sensitized rabbits sacrificed after the addition of an exciting dose of the antigen. In the current literature Shay, Gershon-Cohen, and Fels suggest that occult liver and gallbladder disease may be responsible for an allergic state. They cite 4 cases of chronic urticaria completely relieved by cholecystectomy; in 3 of these patients the gallbladders contained stones. Goss likewise reported 2 cases of chronic urticaria cured by removal of the gallbladder, 1 containing stones, the other exhibiting changes typical of chronic cholecystitis. The 2 cases reported hereinafter suggested the possible relationship between residual symptoms and a sensitivity state and provided the stimulus for this investigation.

CASE 1. A 59 year old male, a chauffeur, entered Cottage Hospital on November 2, 1945 with the chief complaints of weight loss and weakness. He had always enjoyed excellent health until approximately 1 year earlier when, after eating a large meal of fried oysters, he experienced severe epigastric pain which required a "hypodermic" for relief; this episode lasted about 2 weeks following which a cholecystogram revealed gallstones. He was placed on a low fat diet which kept him free of pain. However, a progressive weight loss totalling 45 pounds, despite a good appetite was experienced; this was accompanied by increasing weakness. The history was otherwise noncontributory except for sinus trouble and bronchial asthma. Physical examination revealed a tall, slender, but well preserved male who appeared to have lost considerable weight. The skin was not icteric and there was no evident lymphadenopathy. The heart and lungs were negative, except for wheezing throughout the left chest. Blood pressure was 140/90. The lower margin of the enlarged liver was palpated 5 to 6 centimeters below the costal arch. Physical examination was otherwise noncontributory. Red blood count was 3,570,000; hemoglobin, 11.5 grams; white blood count, 6,200; icterus index, 7; amylase, 6 units. Nonhemolytic streptococci were cultured from fluid obtained by duodenal drainage.

On November 11, 1945 the abdomen was entered through a high paramedian incision. The liver was definitely enlarged but smooth. The gallbladder was slightly distended, fibrotic, and contained numerous small stones. The common duct was dilated and contained many millet seed sized stones which were removed with a small scoop and by irrigation. Palpation of the head of the pancreas suggested nodular induration but it was believed that this change was secondary to inflammation and not to malignant disease. The stomach and duodenum were essentially normal. A cholecystectomy and choledochotomy were performed and external biliary drainage established by placing a T tube in the common duct.

Convalescence was uneventful. Nonhemolytic streptococci (predominant) and Escherichia coli were cultivated from the bile. Penicillin, 10,000 units in 5 cubic centimeters of solvent, was injected into the T tube daily. The patient was discharged from the hospital on the 16th postoperative day with T tube in the common duct. Daily penicillin injections were continued for a period of 15 weeks. At the end of this time cultures were still positive for both nonhemolytic streptococci and Escherichia coli. A cholangiogram did not reveal the presence of stones or an obstruction; the T tube was then removed. The patient had gained 12 pounds and was feeling fine. He continued to improve for a further period of 6 months, gaining, in all, 26 pounds. At this time he returned complaining of headaches, postnasal drip, and frequent gaseous indigestion. He had lost 5 pounds. Complete relief followed a course of benadryl, 50 milligrams 3 times a day. Three years later this patient reported excellent health except for an occasional minor upset which could be controlled with benadryl.

CASE 2. A 25 year old obese male was admitted to the Cottage Hospital September 23, 1946 with complaints of severe epigastric and right upper quadrant pain of 3 days' duration associated with nausea. Several similar episodes had occurred over a 5 year period although none was as severe as the present attack. Jaundice had not occurred. He had been rejected for military service after x-ray studies revealed gallstones. The history otherwise was not significant except for occasional attacks of hives. Physical examination indicated an obese young white male who did not appear acutely ill. The heart and lungs were essentially normal and the blood pressure was 120/85. The abdomen was slightly distended; severe tenderness and moderate involuntary "guarding" were elicited over the right upper quadrant; a tender mass could be palpated just below the liver edge. The examination was otherwise not remarkable. Impression was that of acute cholecystitis with possible hydrops. The white blood count was 13,450; red blood count, 5.19; hemoglobin, 15.4 grams; differential, normal. The urine contained a trace of bile. Albumen was 1 plus. The icteric index was 25 and blood amylase was 300 units.

A cholecystectomy was performed September 27, 1946. The distended gallbladder was acutely inflamed and contained 6 dark brown cholesterol and several lighter calcium stones. No other disease was demonstrated. The common bile duct was carefully explored and irrigated; no stones were found. A

T tube was placed in the common duct for external drainage and the abdomen closed. Recovery was uneventful and the T tube was removed on the 10th postoperative day. Patient was discharged on the 11th postoperative day.

Approximately 2 months after surgery patient again began to suffer acute attacks of right upper quadrant pain typical of those experienced before cholecystectomy. On a regimen consisting of benadryl, 50 milligrams 3 times a day, complete relief was experienced. This was gradually reduced to 50 milligrams every night and then discontinued except for such times as he felt he was threatened with an attack. He recently reported that he had suffered no further acute episodes and was in good health.

These experiences suggested a localized allergic condition which in some way was related to the biliary tract disease. The proved existence of residual bacterial infection in the first case together with the clinical and pathological evidence of inflammatory disease in the second pointed to the possibility of bacterial sensitization. Both patients gave a history of allergic susceptibility. Proof of such a relationship might well explain a certain number of the residual syndromes following cholecystectomy. Accordingly, an investigation was planned which would include culturing bile specimens from a large number of patients, preparing bacterial suspensions from the positive cultures, and skin testing the hosts with such vaccines for evidence of sensitization. It was further proposed to examine the histories of the patients for evidence of clinical allergy and to correlate such information with the end results of surgery.

METHODS AND RESULTS

The majority of the bile specimens for culture were obtained at the time of operation before the gallbladder was removed. The specimen was immediately taken to the laboratory where the character of the specimen was recorded and 1 milliliter was transferred to thioglycolate broth. In this medium both aerobic and anaerobic bacteria may grow. Cultures containing bacteria were subcultured to suitable differential solid media for identification of the organism.

Bacterial suspensions for the skin tests were prepared in the following manner. Four day old cultures in nutrient broth were washed 3 times in saline solution by centrifugation and discarding the supernatant fluid. Merthiolate 1:1,000 was used to kill the bacteria. The suspension was then centrifuged after exposure to the 1:1,000 merthiolate for 18 hours and 1:10,000 merthiolate solution added for preservation. The suspensions were made up to a concentration of 1,000 million to 1,500 million per milliliter and stored in vaccine bottles.

The skin tests were made by inoculating 0.05 milliliter of suspension intradermally into the skin of the forearm on the 10th to 12th postoperative day with a sterile tuberculin syringe. The reaction was observed at 30 minute and 24 hour intervals. Wheal formation, erythema, and induration were used to evaluate the reactions. A reaction was regarded as positive whether the signs were early (30 minutes) or delayed (24 hours) in their appearance. No individuals sensitive to merthiolate 1:10,000 were found.

Results of bile culture are shown in Table I. The results do not differ significantly from earlier published reports of bile bacteriology. Andrews and Henry, reporting one of the latest and largest series, obtained growth in 33 per cent of fluid bile cultures. Branch, in a similar study, reports 40 per cent positive results in culturing fluid bile. These investigators obtained signally higher incidence of positive cultures of the gallbladder wall with correspondingly increasing frequency of the presence of cocci over bacilli. Their results corroborate the contention that the etiologic agents of cholecystitis are principally the streptococcus and staphylococcus and not the commonly reported gram negative bacilli.

Since one of the objectives of our study was to obtain bacterial suspensions for skin testing, it was deemed sufficient to culture only the fluid bile and consequently cultures were made of the gallbladder walls in only 19 cases. It was interesting, however, that in all instances of positive cultures from the walls the fluid bile contained the same organisms (Table I). The percentage of positive bile cultures (30 per cent) is lower than that reported by Andrews and Branch. A possible explanation is that the bile in our cases was removed from the gallbladder before any manipulation and therefore there was little likelihood of bacteria being forced into the lumen from the wall.

TABLE I.—COMPARATIVE BACTERIOLOGICAL STUDIES OF BILE AND GALLBLADDER WALL

Author	Cultures	Cases No.	Positive, per cent	Strepto-cocci, per cent	B. coli, per cent	Staphylo-cocci, per cent	B. welchii, per cent	Other bacteria, per cent
Jennings, Ortega, and Braslow	Fluid contents	149	30	12	12	6	0.7	4
	Wall	19	32	16	16	5		
Andrews and Henry	Fluid contents	106	33	6.5	17.9	4.7		5.6
	Wall	200	89	29.5	26	26	1	18
Branch	Fluid contents	210	40	15	50	18	5	9
	Wall	210	53	11	49	17	8	10
Judd, Mentzer, and Parkhill	Fluid contents	193	14.5	8	6	1	0.5	4
	Wall	200	49	18	4.5	10	1	20
Moynihan	Fluid contents	81	31	37				
	Wall	81	37					
Rosenow	Fluid contents	29	55	17	31			24
	Wall	32	84	56	28		22	22

Reports comparing the incidence of bacilli and cocci vary. Andrews and Henry isolated Escherichia coli in 16 per cent and streptococci and staphylococci in 16 per cent of fluids studied. Branch isolated Escherichia coli in 50 per cent and streptococci and staphylococci in 33 per cent of cases. In our series of cases there were 51 positive cultures of which 18 were streptococci, 9 were staphylococci, and the remaining 24 were in the intestinal bacillary group, or approximately 53 per cent cocci and 47 per cent bacilli. It is to be noted that the streptococci grew even in the presence of a relatively large concentration of bile in the original culture tube, an observation which has been questioned by others.

SKIN TESTS

The limited number of skin tests scarcely warrants percentage evaluation for each of the organisms cultured, but it is of interest that 12 patients with streptococcal infections were followed for a period of 1 year, and of this number 10 (83 per cent) had positive skin reactions. A total of 14 skin tests was performed with the streptococcal suspensions, 7 with the staphylococcal suspensions, and 12 with the Escherichia coli-Proteus vulgaris group suspensions. Of the patients tested with the streptococcal suspensions 9 were definitely positive and 1 was doubtful. Five in the staphylococcal class were positive and 9 patients reacted positively to the gram negative rods present in their gallbladders. Therefore, 74 per cent of the patients exhibited positive reactions to the bacterial suspensions.

In those patients with negative reactions the bacteria present in the bile could reasonably have been there in a transient state, having been carried to the liver via the portal vein and subsequently excreted into the bile or carried by blood or lymphatics, as was observed in 1 case. A patient suffering an attack of acute cholecystitis due to a streptococcus gave a negative skin reaction, the infection in this case not being of sufficient duration to permit tissue reactivity to develop.

It was discovered, however, that in determining the reaction of normal healthy individuals to these suspensions, a majority of them reacted to the suspensions of Escherichia coli and Proteus vulgaris, so that evaluation of the findings in this group is confusing. Controls inoculated with the streptococcal and staphylococcal suspensions showed only a random positive reactor, which is to be expected. Those individuals reacting significantly to intradermal inoculation of killed streptococci or staphylococci can be regarded, therefore, as having either a hypersensitivity or an immunity to that particular strain of organism. The present state of information concerning the relationship between hypersensitivity and immunity will not justify conclusions with respect to the underlying basis for the positive reactions observed. We can

say, however, that those patients showing characteristic skin reactions to the coccal vaccines have had previous infection with the bacterium isolated from the gallbladder contents, which resulted in either hypersensitivity, immunity, or both.

One hundred and forty-nine patients subjected to gallbladder surgery at the Santa Barbara Cottage Hospital during the past 3 years were followed by means of questionnaire or direct contact. Of this number 28 per cent reported residual symptoms and these were classified as unsatisfactory results. In all cases cultures were made of the bile fluid obtained at the operating table by inserting a needle into the gallbladder or common bile duct. The follow-up records were considered adequate in 109 instances. Of these there were 45 positive cultures. The follow-up studies indicated that 76 (69 per cent) had satisfactory results and 33 (30 per cent) unsatisfactory results. Positive cultures were obtained in 30 per cent of the satisfactory and in 18 per cent of the unsatisfactory group. Positive skin tests were obtained from the antigens in 56 and 66 per cent, respectively. Correlation of the end results, allergic history, and skin sensitization to autogenous vaccines is shown in Table II.

In reviewing the hospital records, as well as the returned questionnaires, an attempt was made to separate those giving a definite clinical history of allergy from those with questionable allergy, including food intolerance. Forty-five per cent of the unsatisfactory group were found to have some definite form of allergy in contrast to 20 per cent of the satisfactory group. Adding these to the number with questionable allergy, the figures become 69 per cent of the unsatisfactory group indicating some allergic background in contrast to 42 per cent for the group with satisfactory end results.

There were 18 streptococcal cultures and of these 12 were followed for 1 year; 10 gave positive skin reactions; 42 per cent reported satisfactory results; 41 per cent had some continuing difficulty but were improved; and 17 per cent complained of the same symptoms which they had suffered prior to surgery. A history of clinical allergy was found in 1 and symptoms suggesting allergic sensitivity reported by 3 others.

TABLE II.—ANALYSIS OF 149 CASES STUDIED

	Satisfactory, per cent	Unsatisfactory per cent
Total incidence	72	28
Cases cultured* (109)	69	30
Positive cultures	30	18
Positive skin tests	56	66
Allergy Clinical	28	45
Questionable and food intolerance	14	24
Allergy, Total	42	69

*Of 149 cases cultured adequate follow-up study was obtained in only 109 instances.

The results of an analysis of the entire group with respect to the presence or absence of gall stones indicated that, whereas a higher percentage of positive cultures was obtained from the group with stones, the incidence of positive endermal tests was greatly higher among the noncalculous patients. A history of allergy was recorded more often in the no stone group and the percentage of surgical failures was almost twice that of the cholelithiasis series.

DISCUSSION

The many theories proposed to explain the postcholecystectomy syndrome are proof of their inadequacy. Perhaps the most tenable is the "biliary dyskinesia" or "paralysis of the sphincter" hypothesis. However, the cause of the sympathetic imbalance, or the irritable sphincter, has remained obscure. We believe that the work of Deissler and Higgins approaches a solution to this problem. These investigators demonstrated that in the sensitized experimental animal the addition of the antigen caused a marked contraction in both the gallbladder and the sphincteric mechanism of the choledochus but the resistance offered by the latter was greater than the maximal pressure of the gallbladder with the resultant effect that "the gallbladder contracted but the sphincter did not permit emptying the viscus." Additional evidence supporting the sensitization theory was furnished by Muro and Ficari in their work with sensitized rabbits. Histolo-

gic changes in the gallbladder walls characteristic of an allergic response were seen in all such animals after an exciting dose of the antigen. The controls failed to manifest such changes. These authors concluded that serum proteins are absorbed by the mucosa of the gallbladders of sensitized animals while in the normal animals certain natural barriers prevent this phenomenon from taking place.

For the past two decades it has been recognized that asthmatic episodes may follow infections in the nasopharynx and paranasal sinuses. Cooke induced asthmatic attacks with autogenous vaccines prepared with organisms recovered from the paranasal sinuses and, through antrum "windows," observed accompanying changes in the mucous membranes of the antra which were typical of an allergic state. Thomas maintains that a fairly high percentage of patients with rheumatoid arthritis possess an allergic constitution. He points to the excellent results obtained by desensitization to autogenous bacterial vaccines incriminated after endermal testing. If one accepts the increasing body of evidence favoring a relationship between biliary tract disturbances and an allergic state it would seem reasonable to postulate that such sensitization may result from chronic bacterial infections primary in one of the members of the biliary system.

Most surgeons are agreed that from 10 to 35 per cent of cholecystectomized patients fail to obtain complete relief from symptoms previously attributed to biliary tract disease and that a small percentage experience no relief at all. Judd routinely established external drainage of the ductus choledochus for a period of 3 to 6 months in all cases in which findings at secondary operations were nonrevealing. He believed residual infection was responsible for the persisting cholecystic syndrome in the majority of these patients. The advantage of prolonged drainage was demonstrated in the first of the cases herein reported. This patient remained well throughout the 4 month period of drainage but began to lose weight and complain of symptoms suggestive of biliary tract disturbance, together with those of a nasal allergy, soon after the T tube was removed. Relief of these symptoms following a course of antihistaminic therapy is strongly indicative of an allergic basis. In the second case the postcholecystic attacks were more typical of gallbladder colic and the response to antihistamines more dramatic, but unfortunately proof of chronic bacterial infection was lacking. It may be argued that the relief in both instances resulted from the antispasmodic action of benadryl. Our conclusion to the contrary was influenced by the complete relief from the allergic symptoms which both patients experienced, together with the generally accepted opinion that antispasmodic drugs are of little value in the treatment of the postcholecystectomy syndrome.

The cases included in the present study were taken from 3 surgical services. The number of unsatisfactory results compares favorably with other published studies and, while the percentage is somewhat higher than the majority, it is believed that this is explained by the inclusion of all patients who reported a continuance of symptoms even though improved. The incidence of positive bacterial cultures (30 per cent) likewise approximates that of other investigators. We believe the high percentage of positive skin reactions to the vaccines (76 per cent) is significant. Of the entire series 49 patients (33 per cent) gave a positive history, and an additional 25 patients a questionable history, of clinical allergy. Among the 42 patients classified as surgical failures 45 per cent indicated a definite history of allergy; of this group 31 per cent yielded positive cultures and 21 per cent reacted to vaccination. It will be noted that this incidence is smaller than that for the entire group which may be explained on the premise that the coccal organisms are most commonly associated with an allergic condition; moreover, such infections, as well as metabolic disturbances, in all probability are transient rather than permanent. Rehfuss states that "Cycles of infection may occur precisely as do cycles of hypercholesteremia, resulting in focal involvement and often focal destruction with more or less damage to the organ." His investigations also indicated that the nonhemolytic streptococcus has a high affinity for the biliary appendages; 68.3

per cent of the animals inoculated with one strain of these organisms exhibited some form of gross lesion of the gallbladder although only 8.9 per cent gave positive culture from the bile. In the present study there were 16 cases of nonhemolytic streptococcal infections and of these, adequate follow-up studies were carried out in 12; 83 per cent of the latter group reacted positively to intradermal vaccination.

It is appreciated that such a report leaves many questions unanswered and can serve only the purpose of calling attention to a factor which may explain a certain number of cholecystectomy failures. The higher incidence of unsatisfactory results among the "no stone" patients is in agreement with the reports of most investigators in this field. We were therefore interested to find a greater percentage of positive skin tests and a larger number of patients with allergic histories among this group. These observations should justify the recommendations that all patients suffering with symptoms of cholecystitic disease but whose cholecystograms fail to reveal stones should be carefully assessed for evidence of an allergic diathesis and cultures should be made of duodenal bile. It is also suggested that external biliary drainage be established in all patients operated upon for noncalculous cholecystitis; the bile should be cultured and, when positive, consideration should be given the use of autogenous vaccines. Under these circumstances antibiotic and antiallergic therapy may help in the prevention of postsurgical syndromes.

CONCLUSIONS

1. The incidence of surgical failures in a series of 149 cases studied was 28 per cent.

2. A high percentage of the unsatisfactory results (45 per cent) was found in patients with a definite clinical history of allergy.

3. The postcholecystectomy syndrome occurs more frequently in patients subjected to cholecystectomy for noncalculous cholecystitis. The incidence of clinical allergy was found to be highest and the percentage of skin reactions to autogenous vaccines greatest among this group.

4. Evidence is presented to support the postulate that sensitivity to residual bacterial infection may explain certain cases in which the cholecystic syndrome persists after removal of the infected gallbladder.

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THE INHIBITORY EFFECT OF CORTISONE ON STRICTURES OF THE UROLOGICAL TRACT

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STRICTURE formation is often a major urological disease or complication. These strictures occur in the urethra or ureter. The urethra is a simple, passive tube through which urine courses. The kidney is buffered from the urethra by reason of the interposed bladder with its ureterovesical valves. Urethral strictures therefore usually carry no serious prognosis. These strictures are often of great concern to the patient, however, due to symptoms produced, the ever-present possibility of cystitis, and the discomfort and economic demands associated with their continued treatment.

Per contra, the ureter is an active organ of urinary excretion as a result of its contractions. Ureteral strictures, irrespective of location or degree, often result in serious renal disease. Narrowing of the ureteral lumen prevents adequate urinary drainage. This increased intraureteral pressure is transmitted directly to the kidney and produces hydronephrosis. If unchecked, the condition progresses toward ischemic renal necrosis. As a complicating factor, a hydronephrotic kidney is highly subject to chronic, recurrent pyelonephritis. Minor ureteropelvic strictures often produce massive hydronephrosis. Plastic reconstructions of ureteropelvic strictures, in an attempt to save the kidney, are frequently destined to failure because of secondary formation of scar tissue at the operative site. When such a situation obtains in a solitary kidney, the complication assumes grave proportions. Other ureteral strictures are observed frequently after anastomosis of ureter to ureter or ureter to bladder.

Hydroureter and hydronephrosis following ureterointestinal implantation are, for the most part, attributable to scar tissue deposition about the ureter secondary to the normal healing process. Hinman and Weyrauch have demonstrated experimentally this periureteral concentric fibrosis of the ureter as it traverses the bowel wall. Dean has observed clinically that following ureterointestinal implantation about 20 per cent of his patients required secondary operation for obstruction at the ureterointestinal anastomosis. Fifty-eight of his 98 patients had ureteral dilatation or hydronephrosis or both. Thomas reports 44 per cent of patients in his series developed pyelonephritis following ureterosigmoidostomy. Eleven of 36 patients had ureteral obstruction in one or both sides. Harvard and Thompson report that obstructive phenomena developed in 88 per cent of 144 patients following ureterointestinal anastomosis as determined by excretory pyelography. As a direct consequence of this ureterointestinal disease, 66 per cent of deaths after the patients left the hospital were due to uremia, pyelonephritis with hydronephrosis or stones or both. This incidence of renal disease subsequent to ureterointestinal implantation has been discouraging. Largely on the basis of these statistics and other similar published and personal experiences many urologists have discarded cystectomy for treatment of bladder cancer. The primary purpose of the operation is excision of cancer of the bladder. It is regrettable, but understandable, that the secondary consideration, that of diversion of the urinary stream, should discourage the primary objective.

Some common examples of urethral strictures may be observed at the bladder neck following certain cases of transurethral electroresection of median bar or prostatic hypertrophy. These same surgical procedures produce, not infrequently scarring of the pendulous urethra. Urethral strictures from gonor-

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rheal infection are observed still, but not as often as formerly. Finally, the most carefully performed plastic operation for hypospadias is often complicated by stricture which requires periodic urethral dilatation for many years.

It has been demonstrated amply that infection increases the quantity of fibrous tissue deposition in the healing wound. Hinman has proved that there is a great variance in the stricture resulting from anastomosis of ureter to bladder or ureter to the fecally contaminated bowel. As urologists must contend with urine constantly bathing urethral or ureteral wounds, there is always this potential of infection that will stimulate fibroplasia and contribute to the formation of strictures. In addition, many urological procedures must rely on the use of indwelling catheters for diversion of the urinary stream or to splint anastomoses. These catheters are foreign bodies which per force promote infection and increased fibrosis and scarring at the operative site.

Treatment of urinary tract strictures by the age-old method of dilatation with metal sounds, bougies, or other dilating catheters is unsatisfactory, frequently unending, and certainly not scientific. There is no physiological basis in the concept that repeated stretching of a scar will either lengthen the fibrocytes or imbue them with relaxing capabilities. The present communication reports clinical and experimental observations on the use of cortisone to reduce the formation of scar tissue in urological wounds.

Ragan and co-workers and also Spain and associates have demonstrated inhibition by cortisone of granulation tissue formation in experimentally induced wounds. Subsequent to the initiation of the present investigation, Rosenberg and his group have shown that cortisone greatly diminishes the tendency to scar tissue contracture in experimental esophageal injuries. Stinchfield applied cortisone successfully in preventing excessive fibrous tissue formation after experimental arthroplastic procedures. Physiologically, the mechanism of action of cortisone is probably due, in part, to a local inhibition of fibroblasts and also inhibition of the synthesis of certain mucopolysaccharides by connective tissue cells. Wounds exhibit high capacity for the incorporation of inorganic sulfate into the chondroitin sulfate of granulation tissue. Layton has found that cortisone retards synthesis of this chondroitin sulfate moiety of the connective tissue ground substance.

EXPERIMENTAL STUDY

Procedure. All experimental surgery was performed on healthy adult male or female mongrel dogs, intravenous sodium seconal anesthesia being used while usual aseptic precautions were observed. The experimental animals were divided into two groups:

Group I consisted of 3 dogs that had ureterosigmoidostomy. The ureters were divided low in the pelvis and the distal ends ligated. By a modified Coffey I technique, ureterosigmoidostomy was performed. A generous incision was made through serosa and muscularis of the sigmoid. The ureter entered the lumen of the bowel through a small incision in the mucosa at the distal end of the incision. Three sutures were used to approximate serosa over the ureter. The ureter was thus buried in a trough constructed in an effort to create a ureterosigmoid valve. In order to establish the most unfavorable conditions for healing of ureter to colon, all surgery was performed on dogs with unprepared bowel, i.e., no enemas, cathartics, or intestinal antibiotic agents were used. No specific antibiotic drugs were administered during the postoperative phase of the experiment. Cortisone was administered, 50 milligrams intramuscularly daily, for 3 weeks. The dogs were sacrificed from 45 to 115 days following surgery, and sections were taken of the ureterointestinal anastomoses and kidneys for microscopic examination. Three control animals were managed in like manner but did not receive cortisone.

Group II consisted of 3 dogs that had reanastomosis of ureter to bladder. The ureters were divided at the bladder and the distal ends ligated. The tip of the proximal ureter was split and a single silk suture placed through the splayed end. Needles were then threaded on these sutures and directed through a simple stab wound incision in the bladder and brought out again through the bladder

TABLE I.—TYPES OF STRICTURE STUDIED

	No. cases
Urethral strictures	
Following repair of hypospadias (1 not improved)	4
Postgonorrheal infection	6
Following excision of urethral calculus	2
Posttransurethral surgery (1 not improved)	6
Contracture of bladder neck	
Following resection of congenital contracture	1
Posttransurethral prostatectomy	2
Posttransurethral resection bladder papillomas	1
Ureterovesical stricture	2
Ureterointestinal implantation	2
Ureteropelvic pyeloplasty	2
Total	28

wall 2 centimeters from the incision. Tension on the sutures pulled the ureter into the bladder and the sutures were then tied. No re-enforcing sutures were placed from ureter to bladder other than the one described. None of the dogs received antibiotic drugs. Cortisone was administered, 50 milligrams intramuscularly daily, for 3 weeks. The animals were sacrificed from 45 to 115 days following surgery, and sections were taken of the ureterovesical anastomoses and kidneys for microscopic examination. Three control animals were managed in like manner but did not receive cortisone.

Results. Group I—Ureterosigmoidostomy and cortisone. All dogs in this group had patent ureterointestinal anastomoses. No hydronephrosis was observed irrespective of the time following surgery that the animal was sacrificed. Microscopic examination of the ureterointestinal anastomoses revealed only minimal fibrous tissue deposition at the site of healing of ureter to bowel. The ureterointestinal valve did not appear to be competent. In 2 instances the transitional mucosal pattern of the terminal ureter had undergone glandular metaplasia similar to that in the adjacent bowel. Demonstration of this phenomenon and also the absence of the usual periureteral scarring as ureter traverses bowel wall is presented in Figure 1. The absence of secondary renal injury is demonstrated by Figure 2. One control dog died 4 days postoperatively of a wound abscess (no antibiotic drugs were administered). The remaining control dogs that had ureterosigmoidostomy but did not receive cortisone, demonstrated stricture at the ureterointestinal anastomosis, hydroureter, and hydronephrosis (Figs. 3 and 4).

Group II—Reanastomosis of ureter to bladder and cortisone. All animals in this group had grossly normal ureterovesical anastomoses and kidneys. The control dogs also had normal anastomoses and kidneys.

CLINICAL

Procedure. As a result of the beneficial effects of cortisone on inhibition of fibroplasia observed in dogs, it was decided to extend the investigation to suitable human subjects.

Twenty-four patients with severe urethral or ureteral strictures were treated. An additional study was made of 4 patients who had operative procedures on the urethra or ureter which usually produced some degree of secondary stricture (Table I). No new or different surgery was employed in either group other than the same procedures that had resulted in failure on one or more previous occasions for each patient.

Prior to the present treatment the average number of urological out-patient visits for dilatation of the urethral strictures or bladder neck contractures averaged once every 2 to 3 weeks. All patients studied were admitted to the hospital and were given general anesthesia. The strictures were excised, generously incised, or the scar was ruptured with a large metal sound. A No. 24 Foley bag catheter was used to splint the urethra and also to prevent urinary extravasation. The catheter was removed 3 to 4 weeks following urethral surgery. No catheters were employed in the treatment of ureteral strictures.

Cortisone (cortone), 50 milligrams intramuscularly twice daily, was administered for 2 days prior to surgical manipulation of the stricture and continued for 2 to 3 weeks thereafter. The dosage of cortisone then was gradually reduced and withdrawn completely during the fourth week postoperatively. Antibiotic drugs were administered daily for 4 weeks.

Results. All of the patients studied have been followed a minimum of 6 to a maximum of 9 months after completion of therapy. Of the 24 patients that had severe urethral or

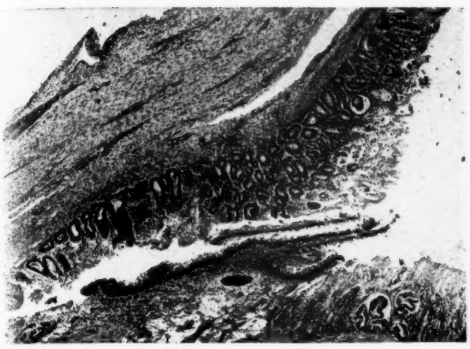

Fig. 1. Dog 162. Cortisone treated. Photomicrograph 145 days following ureterointestinal anastomosis demonstrating minimal scar tissue deposition at the anastomotic site. Note also the glandular metaplasia in the lower ureter. Bowel on the right. × 23.

Fig. 3. Dog 86. No treatment. Photomicrograph 145 days following ureterointestinal anastomosis demonstrating dense fibroplasia about ureter traversing bowel wall. *A*, Ureteral mucosa. *B*, Suture. *C*, Glandular mucosa of bowel. × 12.

ureteral strictures and were treated by cortisone, 22 have been apparently cured. Of the group of 4 patients subjected to surgical procedures that usually produce stricture, none has demonstrated evidence of the development of stricture.

The criteria for cure of urethral strictures usually consisted of marked diminution of signs and symptoms referable to the stricture, absence of residual urine, and maintenance of a large caliber of the urinary stream; ureteral strictures remaining dilated to at least the size of a No. 6 catheter and subsidence of secondary hydroureter and hydronephrosis. None of the 26 patients has required or received dilatation since treatment except for investigational purposes.

CASE REPORTS

Several typical case reports are presented briefly to illustrate the type of stricture treated and the postoperative result.

CASE 1. A 56 year old male was admitted to the hospital with contracture of the bladder neck resulting from transurethral resection of median bar hypertrophy. This operation had been performed 4

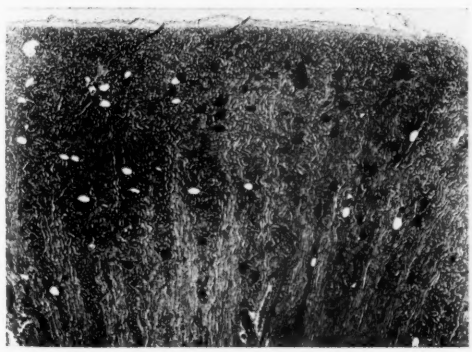

Fig. 2. Dog 162. Cortisone treated. Photomicrograph of kidney 145 days following ureterointestinal anastomosis demonstrating absence of hydronephrosis and pyelonephritis. No ureteral stricture was present. Compare with hydronephrosis illustrated in Figure 4 in untreated dog. × 14.

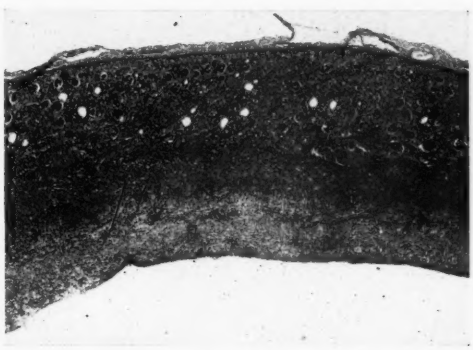

Fig. 4. Dog 86. No treatment. Photomicrograph of kidney 145 days following ureterointestinal anastomosis demonstrating marked hydronephrosis as a result of stricture as ureter traverses bowel wall. Compare with photomicrograph in Figure 2 of same magnification of normal kidney in cortisone treated dog. × 14.

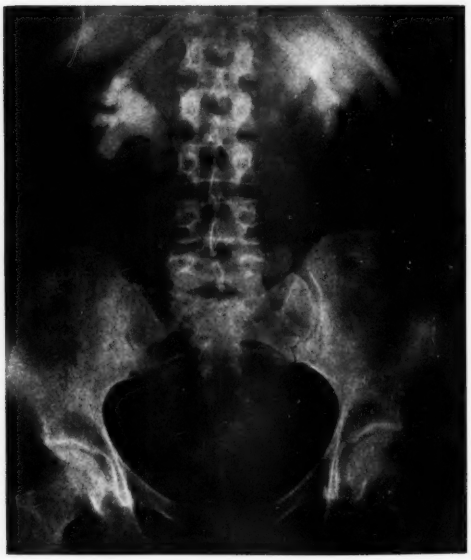

Fig. 5. Case 1. Preoperative intravenous pyelogram demonstrating bilateral hydroureter and hydronephrosis as a result of long-standing bladder neck contracture.

Fig. 6. Case 1. Postoperative intravenous pyelogram demonstrating resolution of hydroureter and hydronephrosis following transurethral resection of bladder neck contracture and administration of cortisone.

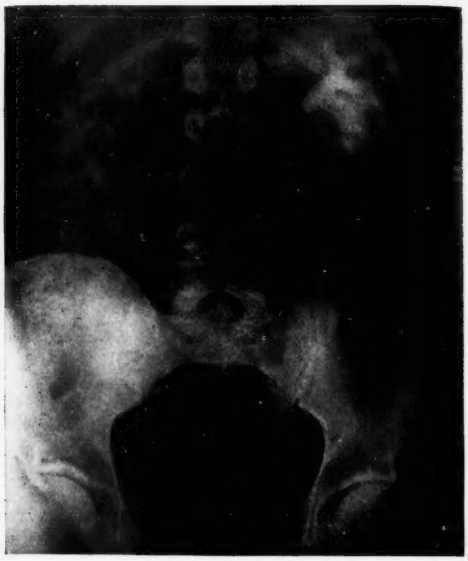

Fig. 7. Case 2. Preoperative intravenous pyelogram demonstrating left hydroureter and hydronephrosis as a result of stricture at the left ureterovesical orifice.

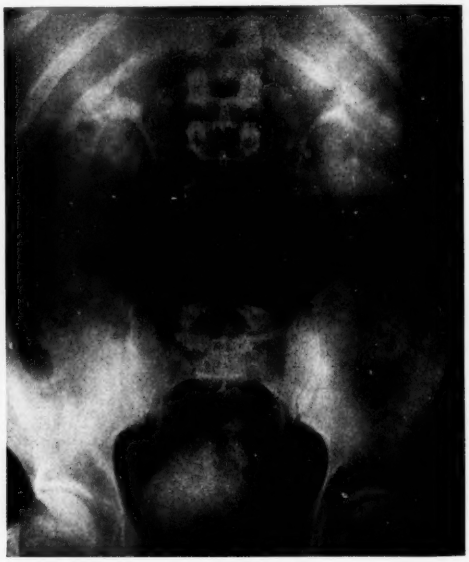

Fig. 8. Case 2. Postoperative intravenous pyelogram demonstrating subsidence of left hydroureter and hydronephrosis following transurethral resection of the left ureterovesical juncture and administration of cortisone.

years prior to admission. Since that time the patient had required dilatation of the bladder neck every 2 weeks. Two previous resections of the scarred bladder neck had been performed without success. The residual urine was 280 cubic centimeters and the symptoms of obstruction were marked. Intravenous pyelograms revealed mild, bilateral, hydroureter and hydronephrosis (Fig. 5). Another transurethral resection of the contracture was performed and cortisone administered as described. Seven months later no bladder neck contracture has re-formed as judged by endoscopic examination, absence of residual urine, nearly complete cessation of symptoms, and intravenous pyelograms demonstrating resolution of hydroureter and hydronephrosis (Fig. 6).

CASE 2. A 53 year old woman was admitted to the hospital with pain in the left flank due to hydroureter, hydronephrosis, and pyelonephritis (Fig. 7). Three years prior to admission the patient had transurethral resection of a transitional cell carcinoma at the left ureteral orifice. On cystoscopic examination a scarred, pin-point left ureteral orifice was observed. Generous transurethral resection of the strictured orifice was performed and cortisone administered. Six months postoperatively the patient is asymptomatic. On endoscopic examination the ureteral orifice is gaping and the hydroureter and hydronephrosis have subsided completely (Fig. 8).

CASE 3. A 9 year old boy was admitted to the hospital with urethral stricture resulting from repair of a penile-scrotal hypospadias. Urethral dilatation had been performed under general anesthesia once each 8 weeks for a total of 3 years. Treatment consisted of extreme urethral dilatation until the stricture ruptured, indwelling catheter drainage, and cortisone. There has been no recurrence of the stricture in 8 months as judged by absence of symptoms and large caliber of urinary stream.

CASE 4. A 64 year old man was admitted to the hospital with a urethral stricture of life-long duration resulting from a penile hypospadias. During a 20 year period, 4 plastic procedures had been performed to correct the deformity. The repair of the hypospadias was excellent, but the severe urethral stricture persisted and required dilatation every 2 weeks. A liberal internal urethrotomy was performed, catheter inserted, and the patient given cortisone. The patient has not required any urethral dilatation for 8 months following treatment. The urinary stream has the same large caliber and force as when the catheter was removed.

CASES 5 and 6. These 2 patients were elderly men admitted to the hospital with cancer of the bladder. Cystectomy, lymphadenectomy, and ureterointestinal anastomosis were performed by a modified Coffey I technique. Cortisone was administered postoperatively for 3 weeks. No hydroureter or hydronephrosis has developed in these patients (Fig. 9). The absence of roentgenographic signs of ureteral stricture, i.e., secondary hydroureter and hydronephrosis, is merely presumptive evidence that cortisone was effective in reducing ureteral stricture.

Fig. 9. Case 5. Postoperative intravenous pyelogram demonstrating absence of hydroureter and hydronephrosis 8 months following cystectomy, lymphadenectomy and bilateral ureterosigmoidostomy (Coffey I) and administration of cortisone.

Case 6 died of recurrence of cancer. This patient had only one kidney. Postmortem examination revealed a patent ureterointestinal anastomosis. There was no stricture at the anastomotic site despite construction of a long submucosal trough. The ureter, renal pelvis, and calyces were normal. The ureterointestinal valve was competent. There was no hydroureter, hydronephrosis, or pyelonephritis (Figs. 10 and 11).

Two patients with urethral strictures treated by the regimen described were not improved. One of these patients had a large caliber stricture of the pendulous urethra resulting from transurethral prostatectomy. Under anesthesia the urethra was easily dilated with a size 28 sound. Only 25 milligrams of cortisone was administered twice daily. The cause for the poor result with this patient was probably due to failure adequately to incise or rupture the scar and also to insufficient dosage of cortisone. The second patient not benefited by treatment had a urethral stricture resulting from repair of a perineal hypospadias. Treatment of this patient was identical to that used for other patients in this study. The explanation for this failure is not known.

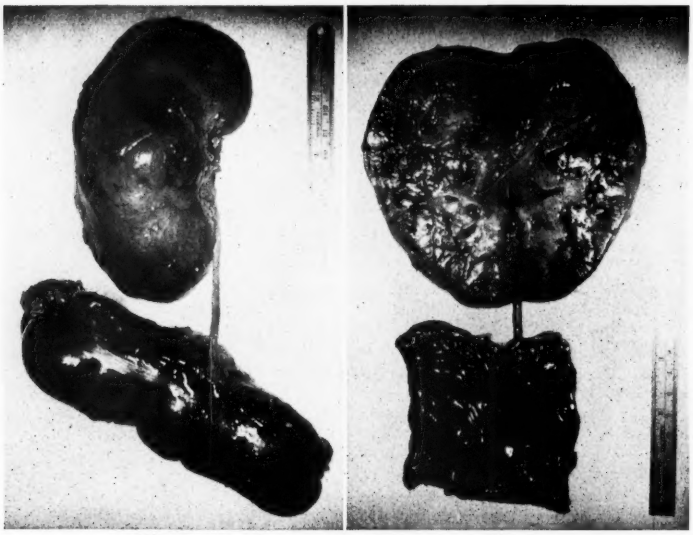

Fig. 10. Fig. 11.

Figs. 10 and 11. Case 6. Postmortem specimen of kidney, ureter, and ureterointestinal anastomosis from a patient with one kidney. Ureteral transplantation had been performed 9 months prior to death. Death was due to recurrence of cancer. Note normal caliber of ureter, normal size of kidney, and absence of hydronephrosis.

Several complications were observed which were attributed to cortisone therapy. One patient with urethral catheter drainage developed epididymitis. This was effectively treated by aureomycin. Another patient had pleuritis 10 years prior to therapy. While receiving cortisone he developed chest pain in the area of the previous pleuritis and the temperature became elevated. An x-ray film of the chest revealed pneumonitis. Penicillin and aureomycin for 3 days caused subsidence of all signs and symptoms. Another complication of cortisone therapy was observed following repair of hypospadias. The skin sutures were removed on the tenth postoperative day and the wound opened, requiring secondary closure. The recommended time for removal of sutures from all wounds is 3 weeks for patients receiving cortisone. Three patients with indwelling catheters developed marked crystalluria. The crystals were of uric acid and urate type. Acidification of the urine accomplished by parenteral use of ammonium chloride cleared the urine of all crystals in several hours.

DISCUSSION

Cortisone apparently has a definite use in the treatment or prevention of strictures of the urethra or ureter as determined by the beneficial effect observed in 26 of the 28 patients studied. The clinical and experimental data presented indicate a decrease in the deposition of fibrous tissue in the healing of urethral or ureteral wounds during the administration of this drug.

The use of cortisone following ureterosigmoidostomy in dogs markedly depressed the production of scar tissue about the ureter as it passes through the bowel wall and thus prevented ureteral stricture and hydronephrosis. It must be emphasized that this obtained despite the presence of infection, as all surgery was performed on dogs that did not have any bowel preparation such as enemas, cathartics, or intestinal antibiotic drugs. The influence of bowel infection on the ureterosigmoid anastomosis when cortisone is withheld is strikingly shown in the control dogs. Each animal had ureterosigmoid anastomotic stricture with secondary hydroureter and hydronephrosis.

Following ureterointestinal implantation and the administration of cortisone in the limited number of humans studied, the results are excellent, but not conclusive. Intravenous pyelograms reveal no hydroureter or hydronephrosis suggestive of a stricture at the ureterointestinal anastomosis. The one postmortem specimen available from a patient who died of recurrence of cancer revealed a decrease in the usual fibroplasia at the ureterointestinal anastomosis. In addition, it was possible surgically to construct a competent ureterointestinal valve. The ureter was of normal caliber and the kidney was normal grossly and on microscopic examination. This beneficial effect of cortisone preventing strictures may be predicted if the experimental data presented are applied to humans.

Certain principles have been learned in the treatment of patients with strictures. All scar tissue must be excised, incised, or actually ruptured if cortisone is to produce optimum results. If no surgical manipulation of the stricture is performed and cortisone administered, the scar will disappear and an apparent cure of the stricture is obtained. Cessation of cortisone therapy, however, causes the stricture to reappear. The crux of the matter involves rupturing or removing the annular scar and splinting the area by means of a catheter so it may heal in a dilated position. Catheters are foreign bodies and tend to promote urethral infection. The function of the cortisone apparently is to reduce the proliferation of fibrous tissue and secondary scarring that is produced in response to infection. All patients should have antibiotic drugs during the period of cortisone therapy; first, to reduce infection to a minimum and thereby modify fibroplasia in the wound; and secondly, because cortisone depresses the immunity of the body by inhibiting the reticuloendothelial system. In the small series of patients studied, urinary tract infections in patients receiving cortisone apparently occur more frequently but respond as well to treatment as in patients not receiving cortisone.

Skin sutures should not be removed for 3 weeks postoperatively in patients receiving cortisone as there is delayed healing of wounds in some instances. To prevent disruption of abdominal wounds it is suggested that steel wire sutures be employed for fascial closure. Twenty-one day chromicized catgut sutures were used for ureterointestinal anastomoses in this study. No ureters failed to heal to bowel when the stated dosage of cortisone was used.

The definitive dosage and duration of therapy with cortisone necessary to produce maximum inhibition of scar tissue is not known, and must be deferred pending further clinical investigation of a larger series of patients, and longer follow-up of the patients who have already been treated.

CONCLUSIONS

1. Cortisone inhibits periureteral stricture and secondary hydronephrosis following anastomosis of the ureter to the fecally contaminated bowel in the dog. The same effect is observed also in humans in the limited series studied.

2. Following reanastomosis of the ureter to the uninfected bladder, there is no appreciable difference in fibroplasia in the ureterovesical anastomosis of the cortisone treated versus untreated dog. The modifying effect of cortisone on fibroplasia is demonstrated best, therefore, in the infected wound.

3. Twenty-four patients have been treated for severe urethral or ureteral strictures by excision, incision, or rupture of the stricture and administration of cortisone. Twenty-two of these patients have maintained normal caliber urethra or ureter, are asymptomatic, and have required no further dilatation. These patients have been followed for 6 to 9 months.

4. Four patients, who had surgery which would usually produce urethral or ureteral stricture, received cortisone postoperatively. No sign or symptom of stricture has appeared 7 to 9 months since cessation of therapy.

5. Urinary tract infections in patients receiving cortisone occur more frequently, but respond as well to treatment as in patients not receiving cortisone.

6. Skin sutures should probably not be removed after surgery for 3 weeks in patients receiving cortisone. The fascia of abdominal wounds should be sutured with steel wire.

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THE SURGICAL TREATMENT OF CHRONIC HIDRADENITIS SUPPURATIVA

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HIDRADENITIS suppurativa, a potentially disabling disease, is a chronic acneform infection of the cutaneous apocrine glands, subcutaneous tissue, and fascia. It is confined to areas in which these glands are found, namely the axilla, the areola of the nipple, the groin, the perineum, the circumanal and the periumbilical regions. In this presentation, an attempt is made to recount the historical landmarks in our knowledge of the cutaneous glands, to clarify the confused terminology applied to the cutaneous glands, and to establish the case for radical surgical excision of chronic infection of the specialized, cutaneous apocrine glands (hidradenitis suppurativa).

History. Velpeau (1839) is credited with being the first to call attention to a "particular circumscribed inflammation and superficial abscess" of the axillary, mammary, and perianal regions. Verneuil, in 1854, suggested that this condition arose in the sweat glands of the skin and, although he described only lesions of the axillary, mammary, and perianal regions, he stated that they may be found wherever sweat glands are found. Availing himself of anatomical contributions of the biologist Robin, Verneuil wrote a number of articles upon this subject from 1854 to 1865. The studies of Charles Robin revealed the anatomical background of the cutaneous glands of man which are involved in the clinical condition of hidradenitis suppurativa.

Prior to Robin's studies (1845), two types of skin glands were recognized. The first were simple tubular sweat glands "rolled into a ball," the ducts of which inscribe spirals as they ascend through the dermis and epidermis to the surface of the skin. The orifices of these glands, found on the cristae of the digits and over the general body surface, were described by Purkinje and Wendt in 1833 and by Breschet and Roussel de Vauzeme in 1834 (cited by Robin). The second type of gland recognized in the skin was the sebaceous gland situated adjacent to the hair follicle and joined to it by a short duct. These compound tuboalveolar glands, discovered by Gurtel in 1835, are found everywhere on the surface of the body except in the hollow of the palm and the sole of the foot. Robin (1845) described a third type, which had not been mentioned before, located abundantly in the subcutaneous tissue of the axilla and in lesser numbers in the perianal region. "It is formed of a simple tube ending in a cul-de-sac and rolled a great number of times upon itself in a manner to form a small lobule which is not rolled as a spiral as found in the sweat glands. The excretory duct is ordinarily larger than the rolled tube which it leaves and constitutes the gland previously mentioned. Sometimes they are united in groups of two or three. They can be seen when one raises the adipose tissue adherent to a strip of skin from the hollow of the axilla. They appear in the form of granulation having a reddish tint or a red color seen sharply against the gray tint of the derma and the yellow of the adipose tissue. These glomeruli are soft and pulpy. Although they have the structure like sweat glands, they are distinguished by the following characteristics: (a) the sweat glands are never joined in groups of two or three nor are they of a reddish color nor visible to the naked eye; (b) sweat glands are seen only with the microscope and they have an excretory duct three or four times smaller in diameter and a glandular mass five to six

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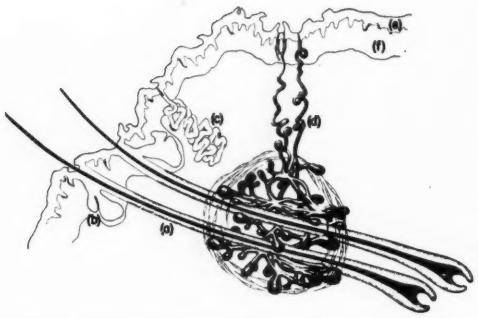

Fig. 1. Schematic presentation of an apocrine gland as constructed from the composite outline of 110 serial microscopic sections cut at approximately 7 micron intervals: (*a*) hair follicle, (*b*) sebaceous gland (holocrine), (*c*) sudoriparous gland (eccrine), (*d*) apocrine gland, (*e*) epidermis, (*f*) dermis. Apocrine gland × 11. Sudoriparous gland × 11 (after Huber, 1) Sebaceous gland × 11. Note the racemose structure of the apocrine gland, its location in a plane deeper to the dermis than the other two types of gland, its relatively greater size, its intimate association with the hair follicle, its tortuous ducts with narrowed meati, and the muscular coat which invests the gland and aids in its secretion. One apocrine gland commonly exhibits more than one duct. Microscopic examination of tissue from cases of hidradenitis suppurativa indicates that the apocrine glands are the starting points of this chronic infection of skin and subcutaneous tissue. The location of the apocrine glands in the subcutaneous adipose tissue, known to be of relatively low resistance to infection and the anatomically inadequate ductile system for the cutaneous discharge of cellular detritus are believed to be the prime factors in the development of hidradenitis suppurativa.

times smaller while these new glands are filled with a granular material not found in sweat glands."

The existence of the so-called "axillary organ" long has been known to biologists and, from studies of this "organ," the general concept of two kinds of sweat glands arose. In 1922 Schiefferdecker described the morphological characteristics of these two types of glands and proposed the terminology which is used today. The simple tubular sweat glands which have excretory ducts opening directly to the exterior and which are not related to the hair follicles he called ekkrine (eccrine, exocrine; krin—secreting). They are found over all of the body but are more numerous on the palmar and plantar surfaces. The compound sweat glands, which are similar to those described by Robin and which constitute the "axillary organ," Schiefferdecker called the apokrine (apocrine) glands. They are found not only in the axilla but also in the areola of the mammary nipple, the mons pubis, the groin, the scrotum, the umbilicus, the perineum, and the anus. These apocrine glands are larger than the eccrine glands and they are compound tubular glands. They are situated more deeply in the subcutaneous tissue than are the eccrine glands and are found only in association with hair follicles. Their ducts open into the cavity of the hair sheath or into the depression in the epidermis near the point where the hair issues. The gland cells are arranged in a single layer and are separated from the basement membrane by a layer of myoepithelial cells which, by contracting, help discharge the secretion. In a single gland the cells may vary from low cuboidal to columnar shape depending upon their state of activity. In general, the more active the cell, the greater is its height.

The act of secretion appears to be accompanied by an accumulation of granules near the surface of the cell which are liberated into the lumen by the rupture and fragmentation of the projecting part of the cell. These secretory granules do not take the ordinary fat stains but they stain light brown with osmic acid. The apocrine glands do not function before puberty. They are recognized as having a definite functional cycle, perhaps related to the menstrual cycle in the female. In certain animals these glands become highly developed, producing strongly scented material, the odor of which may be defensive as in the skunk, or may have a secondary sexual significance as in the musk deer. Homma studied the apocrine sweat glands in white and negro men and women in Baltimore and confirmed Schiefferdecker's findings that the number of apocrine glands is greater in an anatomical specimen of skin from negroes than it is in one from caucasians, the ratio being 3 to 1. Using the Turnbull blue method of staining (counterstaining with alum carmine) he obtained a positive reaction for iron in about 70 per cent of the apocrine glands and no reaction at all in the eccrine glands. Woollard confirmed the findings of Robin, Schiefferdecker, and Homma regarding the phylogenetic significance of these glands in mammals and in man. He describes the

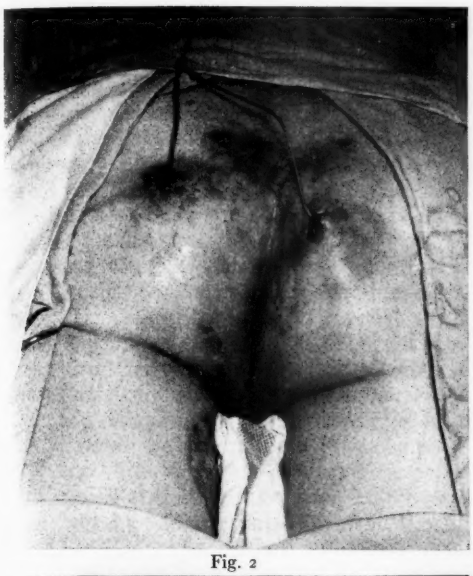

Fig. 2

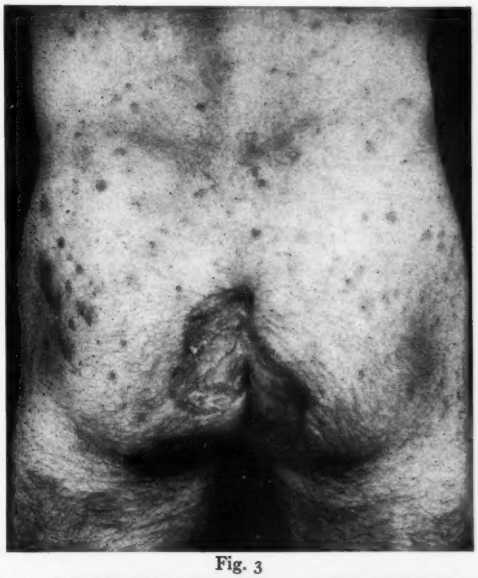

Fig. 3

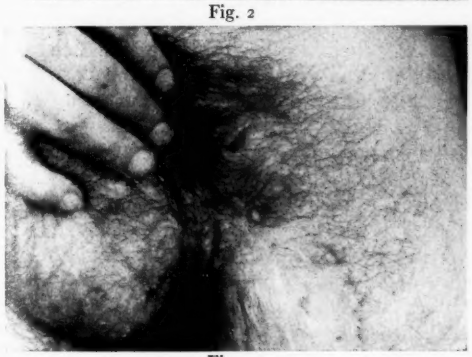

Fig. 4

Fig. 5

Fig. 2. Case 7. Preoperative view of the sacral area of a patient with multiple draining sinuses due to hidradenitis suppurativa. Probes are placed in two sinus orifices. Other openings may be seen medially. All communicated with each other, but did not join other sinuses in the scrotum and perineal region.

Fig. 3. Case 7. Postoperative view of sacral area, showing extent to sacral excision and graft. Note the acneform lesions of the trunk.

Fig. 4. Case 7. Preoperative view of groin, showing sinus openings at level of Poupart's ligament and inferiorly. These communicated with a maze of sinuses in the scrotum.

Fig. 5. Case 7. Postoperative view of perineum, showing extent of scrotal and thigh dissection.

"axillary organ" as occupying the center of the axilla, measuring about 50 millimeters in length, 2 millimeters in width, and 3 to 5 millimeters in thickness. Woollard suggested that the term "anal organ" might apply to the apocrine glands in the circumanal region since they may form a mass 2½ centimeters in width, are analogous to the "axillary organ" in that they are lobulated, compound glands with a fibrous investment, extend deeply into the subcutis, and give a positive iron reaction. These glands, he maintains, are the same circumanal glands described in all textbooks of anatomy.

Anatomical study of the apocrine gland. Serial sections cut upon normal axillary tissue were used to reconstruct a normal apocrine gland (Fig. 1). One hundred ten serial micro-

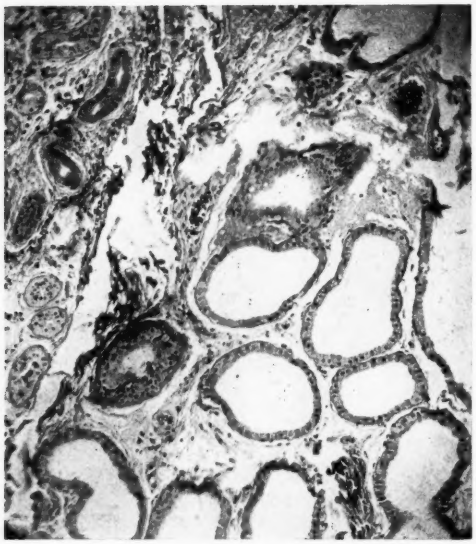

Fig. 6. Photomicrograph showing apocrine glands in uninvolved portion of axilla. Secretory portion of gland at right, ducts at left. × 74.

scopic sections (cut at intervals of 7 microns) were outlined by patterns. The third dimensional structure of the apocrine gland then was composed from these patterns. This gland lies in the deep subcutaneous tissue, well below the skin. Its overall length is approximately 0.3 inch of which 0.12 inch comprise the ductile apparatus and 0.18 inch, the secretory tubules. The latter may be as much as ten times larger in diameter than the ducts. The secretory tubules branch, often many times, and their acini may recoalesce after branching. These tubules are lined with cells whose nuclei stain palely and which vary in size from cuboidal to columnar. Usually the acini themselves are partly filled with granular material, the secretory product of cellular disintegration. Outside the tubules is a thin coat of muscular cells which aid secretion by contracting. The ductile system is comprised of one or several ducts which spiral and coil toward their orifices. These may be connected with a hair follicle or may lie within a deep invagination of epidermis. The cells of the duct stain darker than those of the acini and are arranged in a double row of cuboidal cells. Apocrine glands are in close proximity to hair follicles and these may traverse the gland. The development both of terminal hairs and of apocrine glands at puberty suggests a close developmental origin.

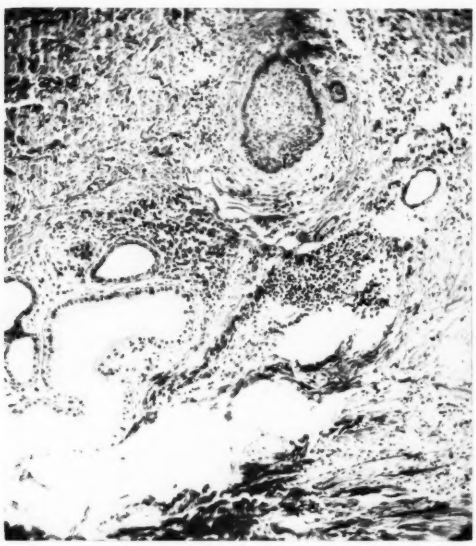

Fig. 7. Photomicrograph showing early acute inflammation around apocrine glands. × 74.

Classification. No single method of classifying the cutaneous glands is entirely satisfactory. However, the following table may aid to clarify the terminology of cutaneous glands:

1. Sweat glands—eccrine—modified simple tubular glands. Secretion without loss of protoplasmic substance.
2. Circumanal, axillary, areolar, inguinal, scrotal, perineal, sacral, umbilical—apocrine—branched tuboalveolar glands. Secretion with loss of protoplasmic substance from the cell.
3. Sebaceous glands—holocrine—compound tuboalveolar. Secretion consists of altered cells of the gland itself.
4. Modified types: (a) tarsal glands of the eyelids; (b) ciliary glands of the eyelids; (c) ceruminous glands of the auditory canal; (d) preputial glands.

Terminology. Prior to 1922 the medical literature (particularly the German) upon the subject of chronic infection of the sweat glands was voluminous. There was recognition of the distinction between sweat gland infections of infants and young children as compared to adults, but the underlying anatomic basis was not understood. Velpeau (1839) described the axillary lesion, now

known as hidradenitis suppurativa, as "abcès tubéreux de l'aisselle," the mammary lesion as "abcès de l'aréole," and the perianal lesion as "abcès tuberculeux ou hemorrhoidaux." Verneuil, in 1864, first used the term "hidrosadenite phlegmoneuse." This condition is confused with furuncle, pyodermia in children and adults, and more recently with chronic undermining burrowing ulcer, nonspecific granuloma, fistulous disease, and pilonidal sinus.

The typical lesion. Verneuil's description of the clinical appearance and progress of the disease in the axilla is still useful. "At first: a slight mobile subcutaneous induration, rolling under the skin and between the fingers; spontaneous pain and pain on light pressure; very little or no elevation; no appreciable redness. This lasts 3 or 4 days. Then the tumor gets larger; advances to the skin which in its turn is inflamed and becomes adherent, a slight redness is seen and pressure becomes painful. Some spontaneous pains appear and are exaggerated by movement of the arm. The tumor is still very hard; no sign of fluctuation is found; there is only glandular swelling, resolution is still possible, and is not very rare. But suppuration more often follows; the elevation increases in size; the skin becomes thinner and turns a dusky red; the epidermis begins to exfoliate. In the center of the induration a soft spot is seen. The redness extends somewhat. The pain is often sufficiently sharp to bring about immobility of the arm and the difficulty one finds on lifting it from the side of the body makes observation difficult. . . . Fluctuation as mentioned above is difficult to feel because of the small quantity of fluid accumulated. . . . Incisions with a point of the lancet are made at the top of the elevations, a few drops of thick viscous pus come out, escaping in the shape of a flat coherent ribbon like the semiliquid contents of the collapsible tubes of paint used by artists. Immediate relief follows this little operation. A few hours or at the most a day later, suppuration has stopped and only a few drops of viscous serum are with difficulty seen running out. The redness in the center and at the edges fades out. But the induration seems hardly affected by this evacuation.

Fig. 8. Photomicrograph showing the formation of a chronic sinus, lined by squamous epithelium and surrounded by inflammatory infiltrate. This is an effect of long standing infection in apocrine glands. × 74.

It begins to resolve only after 2 or 3 days and as it subsides, follows the same course as during its period of growth; that is, it detaches itself from the skin and becomes free in the subcutaneous tissue where it may be perceived for a long time—10, 15, 20 days or even longer."

In the late and chronic stages, the condition presents multiple, tender, painful cutaneous nodules which may coalesce. The fibrous tissue reaction around these nodules forms firm palpable cords in the skin and subcutaneous tissues with numerous sinuses and walled-off abscesses surrounded by edematous, scarred tissues.

Geber (1885), without differentiating between the various glands, described a typically inflamed sweat gland from the perianal region. He emphasized the chronicity of this particular type of lesion and stated that the suppuration extends far and deep with tortuous tracts which may result in perforation of the rectum producing fistula ani. In one of the cases reported herein, the sinuses undermined the skin of the scrotum bilaterally, separated only by the median raphe

Fig. 9. Case 8. Preoperative view of right axilla showing pigmentation and multiple orifices of sinuses.

which acted as a barrier. This same case showed involvement from Poupart's ligament to the midsacral area (Figs. 2, 4).

In the cases to be cited involving the axillas, deep extensions involved the fascia of the musculature, with the extensive inflammatory reaction causing marked thickening of the fascia, but no invasion of the muscle tissue itself. This fascial involvement resulted in muscle spasm which, when aggravated by motion, caused considerable pain. The protective immobilization due to pain resulted in limitation of motion of the regional joint and the late development of contracture. Significant disability resulted in these axillary cases due to limitation of abduction of the arms. In the perineal cases there was limitation of motion at the hips. In several instances patients were unable to sit for many months because of perineal involvement. Their position of relative comfort was supine, with legs braced on pillows in lithotomy position.

Pathology. The histologic picture of the disease was first described from Jadassohn's Clinic by Lewandowsky (1906). This was well reviewed by Tachau in 1934. The pathologic picture is similar to that seen in any acute pyogenic infection of the skin; the involvement of the apocrine glands establishes the diagnosis. Not all apocrine glands need be involved (Figs. 6, 7). Later in the disease, abscess formation followed by sinus formation may destroy all remnants of apocrine gland structure, making an accurate pathologic diagnosis impossible (Fig. 8). The walls of early sinuses are lined by granulation tissue; later these may become epithelialized, an important factor in deciding upon the best surgical approach (Case 7).

Bacteriology. Cultures of pus obtained from the sinuses have yielded a variety of saprophytic and pathogenic bacteria with a predominence of staphylococci and streptococci in our cases. Organisms of the coliform group were noted in cultures in the perianal cases.

Pathogenesis. Although no single etiologic factor can be singled out as causative, it should be noted that 7 out of our 10 cases showed either active acne or severe acne scars of the face and trunk. An eighth patient displayed severe epidermophytosis and an active chalazion while in the hospital. The remaining 2 cases showed either minor acne scars or none at all. It is possible that local factors such as poor cutaneous hygiene, the use of chemical depilatories, shaving, and excessive sweating may predispose to this infection. Since the secretion of the apocrine glands is thick and granular and the glands have much smaller ducts than acini, the mechanical plugging of ducts may be an important factor. Frequent superficial skin infections in the axillary and perianal regions,

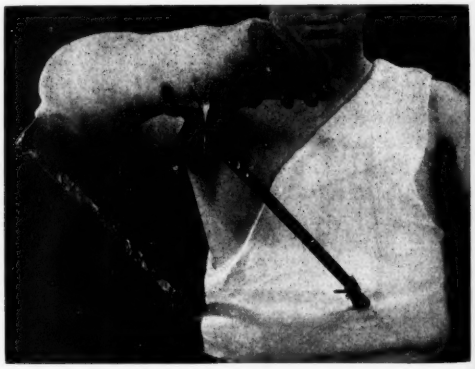

Fig. 10. Case 8. Preoperatively applied immobilization device of plaster-of-paris consisting of two pieces: a Velpeau jacket and an arm splint. Following surgery upon the axilla, the two pieces are incorporated into one device for immobilization by the addition of perforated metal bars which are bolted into place.

skin rubbing against skin, abnormal warmth and moisture from perspiration, all are factors which predispose toward the development of hidradenitis suppurativa.

Diagnosis. This disease entity has failed to receive proper emphasis in clinical practice. As an illustration of its frequency, Jackman and McQuarrie mention 388 cases diagnosed at the Mayo Clinic in a period of 8 years. Increasing reports are calling attention to this entity. The diagnosis rests upon clinical findings of cutaneous nodules and subcutaneous inflammation of a chronic nature characterized by multiple abscesses, draining sinuses, and contracture due to subcutaneous fibrosis in regions where apocrine glands are found. In early cases little disability is present, and as a result no statistical data have been published regarding the incidence of the disease. In cases of short duration biopsy may be helpful as the characteristic histologic appearance of the apocrine glands may still be recognizable. Biopsy can be done at the time of incision and drainage. When the disease is of longer duration, acute and chronic infection may have obscured the microscopic anatomy by destruction of the apocrine glands.

Treatment. Brunsting (1939) concludes that either surgical excision of the involved area or x-ray therapy may be effective for early cases. It should be noted that 7 of our 10 cases had previous x-ray therapy prior to admission to the service. In 1 case, the patient gave the history of spread of the lesions during the course of x-ray treatment. Vaccines, topical applications, and ultraviolet therapy have not been found to be effective. Lane

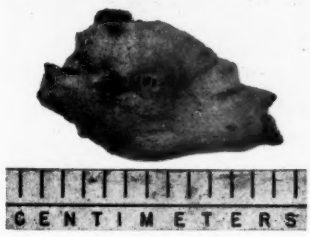

Fig. 11. Case 8. Operative specimen of axillary skin and subcutaneous tissue showing sinuses, pigmentation, and ulceration.

Fig. 12. Case 8. Postoperative view of axilla with graft in place.

(1933) reported cures after surgical intervention consisting of incision, undermining skin flaps, curettage, and packing of the wound. He cited Verdi's personal communication of cures following this method of treatment. This treatment is not favored by the authors because its success depends on healing by second intention with the fibrosis and contracture subsequent thereto.

From our experience with the most severe cases, the chronic cases require radical and complete excision of the inflammatory area, with surgical closure of the defect by the application of a thick split graft of skin. Simple unroofing or exteriorization of all burrowing sinuses has proved inadequate and has resulted in scar formation and contracture. Frequently, several smaller sinuses are overlooked and the patient must return for a second surgical procedure which could have been avoided if the primary excision had been radical and complete, rather than one of simple exteriorization. Exception to this rule is seen in our case of scrotal involvement (Case 7) in which the sinuses were found completely epithelialized, were limited in their ramifications by the median raphe and the intercrural fascia, but intercommunicated so frequently that a simple unroofing left a smooth epithelialized surface, punctuated only by an occasional bridge between roof and floor. Although simple exteriorization was sufficient in the scrotal region in this case, the adjacent groin, perianal region and sacral region of necessity were excised widely and surfaced with thick-split grafts of skin (Figs. 2, 3, 4, 5).

Fig. 13. Case 4. Preoperative view of pigmentation and filtratic nodules of the inner thigh in a patient whose infection was of 6 years' duration.

Fig. 15. Case 4. Postoperative view of the inner thighs and perineum showing the extent of the graft which had been applied.

In a few of our early cases the diseased tissue was excised radically from the axilla and from the perineum. The areas were dressed with physiological saline and skin grafting was done 3 or 4 days later. Later experiences led to the adoption of immediate skin grafting as a better procedure. No untoward difficulties have been encountered when grafts were placed immediately on the supposedly contaminated and often edematous tissues of the base of the excision (Figs. 9 to 15). Postoperative dressings in our experience are a matter of choice. In badly infected cases we have used the open wet technique in which a single layer of wide mesh gauze, anchored by collodion at wound edges, protects the graft from being pulled away as the outer compresses of sterile saline solution are changed every 4 hours for 5 days. In cleaner cases, we have not hesitated to cover the skin graft with xeroform gauze and to apply pressure bandages. Equally good results have been obtained. An important adjunct, not only in the success of the transplant through adequate immobilization but also in the provision for maximum comfort of the patient, is the use of preoperatively applied plaster shells. For the perineal cases a bivalved spica cast is applied with the patient in lithotomy position several days before surgery. This facilitates dressing changes if the open wet technique is used. In axillary cases, preoperatively applied casts to the trunk and arm utilizing adjustable metal bars such as described by Stark are extremely helpful since they can be adjusted to maximum abduction of the arm at the close of the operative procedure after cicatricial scars have been excised and muscle spasm has been overcome (Fig. 10).

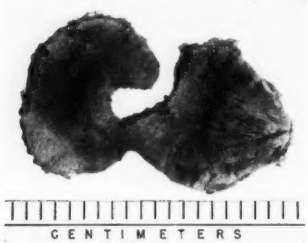

Fig. 14. Case 4. The operative specimen of thigh and perineal skin and subcutaneous tissue. Note the pigmentation and pitting of the sinuses.

Presentation of cases. Since the essential findings and course during treatment are similar in most of the cases of hidradentis suppurativa managed to date, only 2 cases will be presented in detail to illustrate methods used. The first patient illustrates the treatment in our most extensive cases of perineal involvement (Case 7) and the second patient illustrates the method we have found most satisfactory in dealing with axillary involvement (Case 8).

CASE 7. R. S., a 25 year old white male was admitted to the Urology Service of the U. S. Veterans Hospital in April, 1950, with the chief complaint of draining sinuses in the genital area of 5 years' duration. Past history revealed that in 1945 a fistula-in-ano was excised. In 1946, drainage from this same area recurred and drained intermittently. In 1948,

additional abscesses appeared over the scrotum and the inner thighs. Additional sinuses appeared above the anus in the sacral area. Treatment with antibiotics (penicillin, streptomycin, bacitracin) failed to check the spread of the disease. During 2 periods of hospitalization (totaling 21 months) many abscesses were incised for drainage. Extensive genitourinary work-ups at that time revealed no abnormalities. Secretions were examined repeatedly for tubercle bacilli and none found. Numerous sinuses were scattered over the surface of the scrotum, the inner aspects of the thighs, the perianal and the sacral regions. On palpation, the scrotum and adjacent tissues were edematous. Firm cords of indurated subcutaneous tissue could be felt coursing from one sinus to the other. There was no evidence of urinary flow from any of the sinus openings. Intravenous pyelograms showed no abnormalities. Numerous acne scars were scattered over the surface of the face, trunk, and arms. The examination was otherwise negative. The patient was referred to the dermatology service where an incision and drainage allowed for the escape of 2 ounces of pus from the left buttock. Penicillin was again given and the sinuses were irrigated daily with bacitracin solution. Culture at this time showed Aerobacter aerogenes. The patient was then transferred to the plastic surgery service where a spica cast was applied from the toes to the lower thorax; it was bivalved preparatory to surgery. On June 23, 1950, a surgical dissection of the sacral area revealed numerous intercommunicating sinuses which appeared to be separate from the perineal group. This area was excised *en bloc* and the defect was covered with grafts of thick-split skin. These were held in place by a single layer of wide mesh gauze which was anchored to the wound margins by collodion, thus allowing the saline dressings to be changed at frequent intervals without disturbing the grafts. The graft healed ideally in the sacral area. On July 27, the entire scrotal and perineal area was dissected. Since the intercommunicating sinuses of the scrotum were well epithelialized, this section was merely "unroofed"; the tissues of the inner thighs, and of the perianal region were excised *en bloc* but no attempt was made to graft at that time because of the degree of infection. Postoperatively the wound was treated with wet dressings for 5 days, after which skin grafts were applied. The edema of the genital area quickly subsided and, after several weeks, the patient was ambulatory. Two months following the patient's initial surgery, he was discharged from the hospital. Follow-up examination 4 months later revealed that the patient was working and had not had any recurrences.

CASE 8. E. K., a 32 year old white male had suffered from severe acne of the face, chest, and back at the age of 13. Because of abscess formation the patient had had numerous incisions for drainage by his local doctor in 1944, 1947, and 1949. Local therapy had been tried in 1949 without benefit. Examination revealed severe facial pitting and scarring secondary to acne. In addition, the right axilla contained many pustular lesions which extended into the subcutaneous tissue. The skin and superficial subcutaneous tissue of the right axilla was excised under general anesthesia, a thick split graft of skin was applied to the defect and the patient's right arm was immobilized in abduction by means of a cast which had been applied before operation. The graft was successful. Follow-up has revealed no recurrence of hidradenitis suppurativa in the axilla after 19 months.

CONCLUSIONS AND SUMMARY

Hidradenitis suppurativa is a chronic acneform infection of the apocrine glands. These tuboalveolar glands lie in the deep subcutaneous tissue in association with hair follicles and are located in the axilla, areola, groin, perineum, perianal and umbilical regions. They begin to function at puberty with cyclical activity which, in females, is thought to be related to the menstrual cycle. Apocrine glands are three times more numerous in negroes than in caucasians.

Acne appears to be a predisposing etiologic factor although poor cutaneous hygiene, hyperhidrosis, and chemical depilatories may play a role. Diagnosis is made clinically upon the finding in the anatomical areas in which these glands reside of cutaneous nodules, chronic subcutaneous inflammation with fibrosis, and multiple abscesses with draining sinuses. Biopsy performed at the time of incision and drainage may establish the diagnosis.

Cures can be achieved in early cases by improved hygiene, incision, and drainage. In cases of long duration, however, radical excision of all pathologic tissue with replacement by thick split grafts of skin has offered the best opportunity to effect a cure. Many of the cases reported herein have been treated for years with various types of topical and systemic medication and by x-ray therapy, but radical surgery alone has effected their cure. The preoperative application of a one or two piece plaster-of-paris cast has simplified the problem of immobilizing the area of disease which in this entity, with its peculiar regional affliction, often is freely mobile.

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IN VIVO EFFECTS OF CLOSTRIDIUM WELCHII LECITHINASE

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THIS study is concerned with the in vivo activity of lecithinase, the alpha toxin of type A Clostridium welchii. Our interest arose from a series of experiments performed in this laboratory in which attempts were made to evaluate the importance of this enzyme in the toxicity of gangrenous appendicitis (6), of intestinal strangulation obstruction (2, 5, 7), and of massive necrosis of the liver (8).

The biochemistry of bacterial toxins was until recently completely unknown. Most of our present knowledge of toxins has been accumulated in the last two decades. The toxins of the gram-positive bacteria have been studied more because they are more distinct entities than the endotoxins of the gram-negative bacteria. The clostridia and cocci have received most of the attention of investigators. During the recent war the work on clostridial toxins was intensified, and as a result these toxins are now fairly well understood. The recognition, by investigators, that some toxins exhibited enzymatic activity has opened up a new approach to the field.

The toxins of Clostridium welchii type A have been extensively studied. The chief lethal component, alpha toxin, is an enzyme whose chemical properties are now well understood. Van Heyningen has supplied a turbidimetric test for the alpha toxin that is rapid and accurate. This test has spurred considerable study of the toxin and the toxin-antitoxin reactions.

Laufman and co-workers have shown that Clostridium welchii lecithinase, which is present in the peritoneal exudate found in acute ileal strangulating obstruction, is not neutralized locally, but reaches the general circulation in an active form. Many tests, however, failed to reveal the presence of the toxin in the peripheral blood of moribund animals with ileal strangulations. The fate of the toxin in the blood stream is unknown. It may be neutralized immediately, or it may be carried in active form to distant parts of the body to exert its effect. Until more is known of the effects produced by slow absorption of the toxin, its importance in ileal strangulation cannot be accurately ascertained.

The general effects of Clostridium welchii type A toxin given intravenously have been established. These are: (1) shock-like state, (2) hemolysis of the red blood cells, and (3) death in a few hours. Zamecnik and associates showed that intravenous or intramuscular toxin may produce a picture with the general character of traumatic shock, fall in blood pressure, and cardiac output. Gordon and associates reported that intravenous injection of the toxin was followed by rapid hemolysis and decrease in total cell volume and an increase in sedimentation rate and cell fragility. No study has revealed the immediate behavior of the toxin in vivo. It is assumed to attack its substrates, but the location of these substrates in the body has not been established, whether colloidal or in the cell membrane.

Our work is concerned with the activity of Clostridium welchii type A toxin, primarily the lecithinase, in vivo.

SLOW INTRAVENOUS INFUSION OF DILUTE CLOSTRIDIUM WELCHII TOXIN

Experimental methods. Clostridium welchii type A toxin, 400 minimum lethal doses per cubic centimeter No. 199 Lederle, was used in these experiments.

Five healthy mongrel dogs were given morphine and atropine premedication and lightly anesthetized with intravenous sodium pentobarbital. Because of the known synergistic action of alpha toxin and nembutal, the anesthesia was maintained as light as possible. The femoral artery was exposed and a 19 gauge needle inserted for obtaining blood pressure and blood samples. The toxin was

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TABLE I.—SLOW INTRAVENOUS INFUSION OF CLOSTRIDIUM WELCHII TYPE A TOXIN

(20 to 30 drops per min.)

Dog No.	Weight kilo.	Toxin MLD/kilo.	Toxin demonstrated after		Terminal hematocrit
			hours	MLD/kilo.	
1	6	241	2	100	0
2	9	161	3	133	6
3	5.4	100	5	92	14
4	7.1	75	—	—	20
5	14.5	50	—	—	6h/21

diluted in approximately 200 cubic centimeters of normal saline and administered slowly in the opposite femoral vein. Blood pressure, pulse, respiration, and hematocrit readings were made at regular intervals, as well as plasma lecithinase determinations.

In 2 animals serum total and acid soluble phosphorus were followed at regular intervals using the method of Fiske and Subbarow, and the protamine titration was carried out by the method described by Allen.

The blood samples for serum lecithinase determination were collected as for prothrombin time, 1 part 0.1 molar sodium oxalate to 9 parts of whole blood. The cells were immediately spun down, and plasma removed and recalcified. The clot was removed and the serum tested with lecithovitellin solution for lecithinase activity using Tanturi's modification of Van Heyningen's turbidimetric test.

Results. All animals showed marked hemolysis of the blood, which began about 2 hours after the toxin infusion was started and progressed until death. In 3 of the 5 animals toxin was demonstrated in small amounts in the blood approximately 3.5 hours after the infusion began. This corresponded rather closely to the appearance of hemolysis. It was noted that the toxin concentration injected had to be 100 m.l.d./kilogram or above before it was demonstrable in the blood. In the 2 dogs in which the toxin was not demonstrable total and acid-soluble phosphorus studies showed that both of these had increased. The total phosphorus increased approximately 15 to 20 per cent and the acid-soluble fraction increased 56 per cent and 80 per cent respectively. This would suggest that there had been considerable enzymatic action by the toxin in these animals although the toxin had not been demonstrable by the test (Tables I and II).

The blood pressure usually remained constant up until 30 to 60 minutes before death, whereupon it fell to 30 to 40 millimeters of mercury and remained at that point until death. Pulse and respiratory rate gradually increased until death.

Postmortem examination of these animals showed multiple hemorrhages in all organs, and hemorrhagic effusions of the serous cavities. The majority exhibited retroperitoneal and perirenal hemorrhages. Excess bleeding from puncture wounds and other minor injuries was striking.

The protamine titration was found to be increased slightly in both animals tested after the fourth hour.

EFFECT OF SUBLETHAL DOSE OF CLOSTRIDIUM WELCHII TYPE A TOXIN IN VIVO

The response of the formed elements of the blood—platelets, leucocytes, and red blood cells—to sublethal doses of alpha toxin, as well as the change in the clotting activity of the blood was followed.

In 2 animals a complete bone marrow study was made by Dr. Henry E. Wilson.

Experimental methods. Nine healthy adult mongrel dogs were lightly anesthetized with nembutal and given Clostridium welchii type A toxin intravenously (sublethal doses—15 to 40 m.l.d./kilo.). The platelet count, hematocrit, antilecithinase level, and whole blood clotting time were followed at short intervals.

A glycerated Clostridium welchii type A toxin No. 213-2, which contained 400 m.l.d./c.c. (mouse) was used. The dose was measured in a tuberculin syringe and then diluted in about 20 cubic centimeters of normal saline. In each case the toxin was administered intravenously in the foreleg of the dog, taking approximately 5 minutes to give the injection.

Blood samples for platelet, red blood count, hemoglobin, and white blood cells were taken from the femoral vein, which was exposed through a small incision. An 18 gauge needle was inserted and a specimen collected in a 2 cubic centimeter syringe for platelets; the

specimen of blood for the clotting time obtained next; then an oxalated sample for hematocrit and antilecithinase.

One and one-half cubic centimeters of blood for the platelet count was drawn into a 2 cubic centimeter syringe and gently rotated to mix the fixative with the blood. The count was made in approximately 2 hours. A normal platelet count for dogs using this method was 130,000 to 200,000 per cubic millimeter.

Approximately 5 cubic centimeters of blood for the whole blood clotting time was drawn into a 10 cubic centimeter siliconized syringe and immediately 1 cubic centimeter of blood was placed in each of 3 acid-clean coagulation tubes (8 mm. by 75 mm.). These tubes were allowed to set for 10 minutes without disturbance and then the first tube was gently tilted every 60 seconds until it clotted. As soon as it clotted the second tube was tilted until coagulation and so on with the third. The coagulation time was taken as the time it took for the third tube to become coagulated. The normal coagulation time using this method varied from 20 to 45 minutes for apparently healthy and normal dogs. The results obtained were rechecked on numerous occasions and coagulation rechecks seldom varied more than 1 to 2 minutes for long coagulation (35 to 40 min.).

The hematocrit was determined by standard method using Westergren tubes.

Antilecithinase determinations were made by a technique described by Tanturi and associates (8). The blood was oxalated as for prothrombin time and exactly recalcified with calcium chloride. After coagulation occurred the serum was used for antilecithinase study.

The protamine titration was performed in one case using Allen's method. Two large healthy normal mongrel dogs were given 20 and 30 m.l.d./kilo. of Clostridium welchii toxin intravenously, respectively. Red, white, platelet and reticulocyte, and differential leucocyte counts were made. Marrow smear with supravital stain and marrow counts were performed. The hematocrit was followed. These studies were repeated at 2, 4, and 24 hours after injection. One animal died after 48 hours; the other survived without untoward effects and the study was repeated in 1 month.

TABLE II.—SLOW INTRAVENOUS INFUSION OF CLOSTRIDIUM WELCHII TYPE A TOXIN
(20 to 30 drops per min.)

Dog No.	Protamine titration	Total P initial	Total P terminal	Acid-sol. P initial	Acid-sol. P terminal	Acid-sol. P 3h. incub.
4	.16 (at 5h)	11.3	16.2	4.6	8.3	12.2
5	.20 (at 4h)	14.1	16.7	2.8	4.4	5.7

Results. The most striking feature observed in these experiments was the early precipitous fall of platelets. In most instances the number of platelets fell to less than 50 per cent of their initial value in the first 2 minutes after injection of the toxin. The fall in number continued for approximately 1 hour and reached a level 10 to 20 per cent of the initial level by 1 hour. No platelet clumps were noted in making the counts, but debris was frequent. Occasionally very large irregular platelets were noted after 2 to 3 hours. Some of these measured 30 to 40 microns by 4 to 5 microns. The platelet counts rose from the second to seventh day after the toxin. Usually at the seventh day the count approached the original value (Table III and Fig. 1).

There were marked changes in the clotting time; some of these paralleled the changes noted in the number of platelets. The clotting time fell rather abruptly in the first few minutes (2 to 5 min.) after the toxin. This was followed by a prompt rise that approached the initial value. The clotting time then gradually increased, reaching a peak in 2 to 3 hours that was considerably above the initial value. In the next 6 hours the clotting time gradually fell, reaching a point about 75 per cent of the initial value. The clotting time usually returned to normal value 4 to 6 days after injection of the toxin (Fig. 2).

The hematocrit values remained about the same in this experiment. Occasionally they were depressed approximately 20 per cent of the original value.

The protamine titration was found to be elevated in 15 minutes (Table IV).

Antilecithinase values were not changed appreciably. A minor rise was consistently noted 2 to 3 hours after the toxin was given.

The bone marrow showed little effect of the toxin in 30 minutes. The first change noted

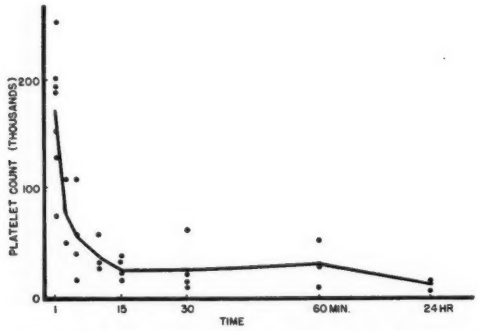

Fig. 1. Platelet count after intravenous Clostridium welchii type A toxin (scatter curve—6 animals).

TABLE IV.—CHANGE IN PROTAMINE TITRATION IN DOG FOLLOWING INTRAVENOUS CLOSTRIDIUM WELCHII TYPE A TOXIN (20 MLD/KILO.)

Dog No.	Time (min.)	Protamine titration
12	Initial	.10
	Toxin: 20 MLD/kilo.	
	5	.10
	10	.12
	15	.18
	30	.18
	60	.18
	180	.18

at this time was phagocytosis of erythrocytes by macrophages of the marrow. There was a decided change in the marrow after 2 hours. Numerous phagocytic clasmatocytes containing recognizable red blood cells and debris were seen. There was also some tendency to hydropic degeneration of the myelocytes. Some isoagglutination was noted in the vital preparations. There was an increase in the number of mitotic figures in the nucleated erythroid elements (Tables V and VI).

At 24 hours the bone marrow showed a marked quantitative reduction in all cellular elements. Numerous monocytes and clasmatocytes were seen containing ingested pigment and lipid material.

Twenty-two days after injection there was a relative erythroid hyperplasia and all the iron containing clasmatocytes were noted to have disappeared.

TABLE III.—SUBLETHAL DOSES CLOSTRIDIUM WELCHII TOXIN INTRAVENOUSLY PLATELETS (THOUSANDS)

Dog No.	Toxin MLD/ kilo,	Time — minutes						
		Initial	2	5	10	15	30	60
1	40	154	—	—	—	—	16	12
2	35	202	—	—	—	22	24	—
3	17	190	50	16	32	32	—	30
4	15	108	64	114	84	76	112	Died
5	15	166	150	164	142	136	120	—
6	25	256	110	110	30	16	24	—
7	20	Specimen ruined						
8	20	76	20	40	34	22	14	10
9	20	130	76	58	60	40	64	50

RATE OF HYDROLYSIS OF LECITHIN IN VIVO BY CLOSTRIDIUM WELCHII ALPHA TOXIN

The progress of the hydrolysis of plasma lecithin was followed by serial determinations of total and acid soluble phosphorus in nephrectomized dogs.

Experimental methods. Dogs were lightly anesthetized with ether and bilateral nephrectomy performed. The serum total and acid-soluble phosphorus was determined before the procedure and after the animals regained consciousness. The toxin (Clostridium welchii type A No. 213-2, 400 m.l.d./c.c.—mouse) was injected intravenously. One animal was given 200 m.l.d./kilo., a massive dose; and 2 animals were given 40 m.l.d./kilo., a borderline lethal dose. The serum total and acid-soluble phosphorus were followed every hour, using the Fiske and Subbarow method.

Results. The dog receiving the massive dose of the toxin (200 m.l.d./kilo.) died 2 hours following injection. The total phosphorus was not significantly changed, but the acid-soluble phosphorus gradually rose to a level 136 per cent above its initial value.

One dog receiving 40 m.l.d./kilo. showed little change in the total or acid-soluble phosphorus, but expired 3 hours following administration of the toxin. The other animal receiving 40 m.l.d./kilo. lived 5 hours and showed a slow, progressive rise of both total and acid-soluble phosphorus (Table VII).

TABLE V.—CHANGE IN DIFFERENTIAL COUNT AFTER INTRAVENOUS CLOSTRIDIUM WELCHII TOXIN

Dog No.	Time	Differential count					
		Bands	Seg.	Lymph	Mono.	Eos.	Bas.
10	Initial	4	74	11	8	3	0
	2 hours	16	65	2	7	8	0
		(6 nucleated RBC, 1 promyelocyte, large platelets)					
	24 hours	20	72	3	4	1	0
		(14 nucleated RBC)					
11	Initial	2	58	32	8	0	0
	2 hours	26	51	13	6	4	0
		(14 nucleated RBC, 4 large platelets)					
	24 hours	32	61	3	1	1	0
		(4 nucleated RBC, 1 eosinophilic myelocyte, 1 metamyelocyte)					

DISCUSSION

The toxin was demonstrable in the peripheral blood only after massive doses had been infused and then only minute amounts of the toxin could be detected. Its presence in the circulating blood is evidenced by progressive hemolysis and gradual increasing acid-phosphorus content of the blood, although tests for the toxin itself are negative. This inability to demonstrate the circulating toxin is difficult to explain. However, a number of factors could prevent its detection. These inhibitory factors are: (1) antitoxin, (2) adsorption on erythrocytes, leucocytes and endothelial cells, (3) inhibition by products of hydrolysis, (4) adsorption on lipoid particles, (5) combination with substrate, thus making it unavailable for the test, and (6) fixation by tissues. The relative importance of these factors in the destruction or inactivation of the toxin awaits further investigation. There is some evidence to show that the cells play considerable role in the inactivation of the toxin. This is probably a tissue fixation effect—possibly neutralizing enzymes are liberated upon the lysis of cells. Fixation to cellular stroma is quite important, however. It is very likely that if these inhibitory effects are better understood, the mechanism of defense and possibly the fate of the toxin could be clarified.

Clostridium welchii type A toxin introduced intravenously produced rapid hemolysis followed by collapse and death in a few hours. This was accompanied by multiple hemorrhages into serous cavities and organs. The tendency to hemorrhage was very prominent. Many workers have described the hemolytic properties of the toxin; however, none have discussed the hemorrhagic phenomena that accompany its action. Tanturi and Anderson noted that in lethal doses their dogs showed decreased prothrombin concentration which may reach hemorrhagic levels. Zamecnik and associates also noted decreased prothrombin and also poor clotting of the blood in the terminal phase of the intoxication.

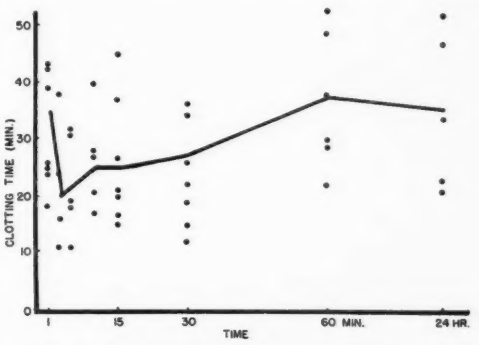

Fig. 2. Clotting time after intravenous Clostridium welchii type A toxin (scatter curve—7 animals).

This study indicates that the cause for the hemorrhagic tendency is apparently a very complicated one. The following factors are to be considered involved in the production of the over-all picture of the hemorrhagic state: (1) a marked diminution of platelets, which

TABLE VI.—EFFECTS OF INTRAVENOUS CLOSTRIDIUM WELCHII TYPE A TOXIN ON CELLULAR ELEMENTS OF BLOOD

Dog No.	Time	RBC $\times 10^6$	WBC $\times 10^3$	Marrow count $\times 10^3$	Hematocrit
10	Initial	7.9	15.8	85.2	55
	2 hours	6.0	8.3	151.0	51
	4 hours	6.2	15.2	20.0	41
	24 hours	4.8	31.3	16.0	37
11	Initial	5.86	8,0	94.0	47
	2 hours	5.51	11.6	Clotted	44
	4 hours	8.00	6.9	42.0	46
	24 hours	4.37	43.6	Clotted	32

TABLE VII.—SERUM PHOSPHATE COMPARTMENT CHANGES IN NEPHRECTOMIZED DOG FOLLOWING CLOSTRIDIUM WELCHII TYPE A TOXIN

Dog No.	Toxin MLD/kilo.	Initial		1		2		3	
		TP*	AP**	TP	AP	TP	AP	TP	AP
6	200	20.0	7.2	27.1	10.9	21.6	17.0		
7	40	23.2	6.5	20.6	3.5	18.8	4.0	Died	
8	40	26.3	8.5	24.4	9.6	20.6	8.5	34.4	21.0

* Total phosphate
**Acid phosphate

makes its appearance very early, (2) alteration of the clotting activity of the blood, (3) liberation of heparinoid substances, (4) damage to the capillary endothelial cells throughout the body, (5) toxic influence on the liver, and (6) alteration of the plasma proteins.

The reduction of the number of platelets present in the circulation appears immediately upon introduction of the toxin and progresses for some time. Absence of clumping of the platelets with observation of excess platelet debris would indicate that the platelet lysis occurred without clumping. Another point noted was that the effect on the platelets was always immediate with all doses, where an effect was observed. No delayed-action effects were noted. Serial observations indicated that the platelet count remained depressed for from 4 to 6 days. These observations indicate that a very early action of the toxin is to destroy the circulating blood platelets, presumably by direct action on the cellular wall or cytoplasm. The fact that the platelet count returned to normal in 4 to 6 days would indicate the megakaryocytes were not affected by the toxin in the dosages used. This action on the platelets is the earliest effect of the toxin noted.

The change in the clotting time at first parallels, and may be related to, the change in the platelets. A sudden release of thromboplastin from the platelets probably lowers the clotting time abruptly. Following this, the clotting time slowly returns to normal. The rise in clotting time observed during the period from 30 minutes to 2 hours is probably due to effect of the enzyme on tissue, with cellular destruction, release of heparinoid substances, intracellular enzymes and proteins. Upon excretion or neutralization of these substances the clotting time returns almost to normal. The clot is, however, still impaired. At this stage it is usually soft and friable, probably because of the low platelet content and a decrease in fibrinogen.

Damage to endothelial cells of the capillaries undoubtedly represents an important factor in the hemorrhagic state. Unfortunately there is no test available to estimate this damage quantitatively. Many workers have commented on the endothelial swelling and extravasation of red blood cells. In this study we were impressed with the massive hemorrhagic effusions in the serous cavities and retroperitoneal edema, which we think definitely represents a gross change due to capillary leakage. We also noted on occasions that the hematocrit would appear to rise even though active hemolysis was progressing. This could indicate capillary leakage of plasma which predominated temporarily.

Release of heparinoid substances has not been observed as a constant finding. Tanturi and co-workers (7) were not able to demonstrate an increase. However, Kellaway and Trethewie in perfusion experiments showed that quantities of adenylic compounds were liberated. These are considered "heparinoid." In a few isolated instances we observed a slight, but definite, increase in protamine titration.

Tanturi and Anderson (6) reported that the histologic picture of the liver always showed acute congestion, dilatation of the sinusoids and, in the severe cases, acute necrosis, and hemorrhagic infarcts. The degree of damage undoubtedly varies with the dose of toxin. This damage to the liver results in a hypoprothrombinemia, hypofibrinogenemia, and hypoglycemia. It has been shown that agents which injure the liver tend to render the blood less coagulable and change the chemical composition of the blood as follows: (1) increase in proteolytic ferment, (2) decrease in antiferment, (3) increase in noncoagulable nitrogen, (4) increase in amino acids, and (5) increase in lipase.

The shock which appears following intravenous administration of Clostridium welchii toxin has been considered to be a peptone

reaction. It is true that it has the general character of a peptone reaction but it differs in the following respects: (1) platelets are lysed early without clumping and appear in the plasma only after regeneration, (2) liberation of heparinoid substances does not appear to be pronounced, (3) capillary endothelial damage is extensive, (4) marked toxic effect on all tissue cells, and (5) histamine is not released.

The most prominent changes observed by us in the cells of the peripheral blood following administration of the toxin were (1) hemolysis of red blood cells, (2) transient leucopenia followed by marked leucocytosis. The hemolysis and leucopenia appeared at about the same time. After 24 hours the leucocytosis was well established. At this time the differential count revealed a marked shift to the left, numerous nucleated red cells, immature granulocytes and giant platelets. The damage to the marrow seems to be exerted primarily on the erythroid elements, and at a much later time and/or at a slower rate than damage to the circulating cells.

The changes in the total and acid-soluble phosphorus occur when lytic effects begin; that is, 2 to 3 hours after injection of toxin. The ratio of total to acid-soluble phosphorus shows a change that would indicate action of the circulating enzyme.

SUMMARY

Our study of the action of Clostridium welchii type A lecithinase in vivo indicates the following:

1. Enormous quantities of the toxin may enter the general circulation and yet be undetectable by present means.

2. Circulating undetectable quantities of toxin can carry on hydrolysis of lecithin.

3. The action of the toxin on the cellular elements of the blood is marked. The most dramatic action is the early rapid destruction of the blood platelets; later the red and white cells are attacked.

4. A complex hemorrhagic diathesis follows intravenous injection of the toxin which is not dissimilar from that observed following total body exposure to ionizing irradiations. It is characterized by (a) thrombocytopenia, (b) increased coagulation time, presumably due to circulating anticoagulant, (c) widespread capillary damage, (d) toxic damage of the liver, and (e) alteration of plasma proteins.

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ACUTE ADHESIVE ILEUS

A Study of 412 Cases with Particular Reference to the Abuse of Tube Decompression in Treatment

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THERE still exists the widespread belief that acute intestinal obstruction due to adhesions is ideally suited to treatment by nonoperative intestinal intubation. It must be evident from the start that such a therapeutic concept presupposes the existence of absolute diagnostic criteria for differentiating simple and strangulated obstructions. Is it true that the absence or presence of fever, tachycardia, leucocytosis, a palpable mass, and signs of peritoneal irritation suffice to differentiate these two varieties of obstruction? It should be possible by careful clinical study to put these criteria to the test. It is the purpose of this report to present such a study, directed at evaluating the validity of some of the established criteria.

MATERIAL

A series of 412 cases is reported, including all cases in which the diagnosis of acute adhesive intestinal obstruction was made on all services at the Charity Hospital in New Orleans over a period of 10 years (1940 to 1949, inclusive). The reported cases were of patients who were either admitted with a primary diagnosis of obstruction or who developed it as a complication during hospitalization. Only the cases of those patients are included who were proved by laparotomy or autopsy to have acute obstruction, or, if operation or autopsy was not performed, who presented a clinical picture upon which a positive diagnosis could be established beyond reasonable doubt.

Ninety per cent of the patients in this series had previously been operated upon. Gynecological operations were the most frequent cause of subsequent intestinal obstruction, being responsible for 127 (34.3 per cent) of the cases. Appendectomy ranked second as the precursor of postoperative adhesions causing obstruction, and accounted for 105 (28.3 per cent) of the cases.

If obstruction developed within a period of 4 weeks after an abdominal operation or an episode of peritonitis, the adhesive process was considered a recent or fresh one. In this series 13.9 per cent of the cases were classified as resulting from recent adhesions, and 86.1 per cent from old adhesions (Table I).

The age distribution by decades is presented in Chart 1. The youngest patient was 5 weeks old; the oldest 85 years. Patients over 50 years of age comprise 26 per cent of the material and 51 per cent of the deaths.

Forty-six per cent of the patients were males; and 54 per cent were females (Table I).

Negroes were afflicted more often than whites, the ratio being almost 3:1; while the ratio of negroes to whites in the Charity Hospital population during the period covered by this study was about 3:2.

Obstruction limited to the small bowel accounted for 98.8 per cent of the entire material (407 cases). Cases of large bowel obstruction accounted for only 1.2 per cent (5 cases).

In 60.2 per cent of the cases the obstruction was considered complete, and partial obstruction existed in 39.8 per cent (Table I).

At operation or autopsy 21.3 per cent of the patients were found to have strangulated obstruction. Unless the operator's note specifically mentioned the presence of gross evidence of compromise of the circulation, the case was classified as one of simple obstruction. Bowel resection was required in only 8 per cent of the cases.

One hundred and seventy-three (43.6 per cent) of the patients had had symptoms of

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intestinal obstruction less than 24 hours when admitted to the hospital, whereas the remainder (56.4 per cent) were later cases (Table I).

RESULTS

There were 49 deaths in the series of 412 cases, a mortality rate of 11.8 per cent (Table I). Three patients were moribund on admission, but are included in these totals.

The major factors influencing prognosis were the age and race of the patient, and the site, degree, type, and duration of obstruction (Table I).

Patients over 50 years of age comprised 26 per cent of the material and 51 per cent of the deaths. The death rate of the patients up to and including 50 years of age was 7.8 per cent. Above 50 years it was 23.3 per cent.

Only 6.8 per cent of the white patients died, whereas the mortality rate for the negroes was more than twice as high (13.9 per cent). The mortality in small bowel obstruction was 11.8 per cent; in large bowel obstruction it was 20 per cent. The mortality rates for the patients with partial obstruction and complete obstruction were 3.7 per cent and 17.3 per cent, respectively. Only 6.7 per cent of the patients with simple obstruction died; while the mortality of strangulated obstruction was 30.6 per cent. Fresh adhesions seemed to be more dangerous than old ones. Of the patients seen within the first 24 hours of their illness, only 6.4 per cent died; the death rate was almost three times as great (16.1 per cent) in those who had been ill more than 24 hours.

TABLE I.—ACUTE ADHESIVE ILEUS MATERIAL AND RESULTS

	No. of cases	Per cent of cases	No. of deaths	Mortality per cent
Total cases	412	100.0	49	11.8
Sex				
Male	190	46.1	25	13.1
Female	222	53.9	24	10.8
Site of obstruction				
Small bowel	407	98.8	48	11.8
Large bowel	5	1.2	1	20.0
Degree of obstruction				
Partial	164	39.8	6	3.7
Complete	248	60.2	43	17.3
Type of obstruction				
Simple	324	78.7	22	6.7
Strangulated.	88	21.3	27	30.6
Bowel resection				
Yes	33	8.0	10	30.3
No	379	92.0	39	10.2
Color				
White	117	28.4	8	6.8
Negro	295	71.6	41	13.9
Etiology of obstruction				
Old adhesion	355	86.1	39	10.9
Recent adhesion	57	13.9	10	17.5
Durationofsymptoms*				
Less than 24 hrs.	173	43.6	11	6.4
More than 24 hrs.	223	56.4	36	16.1

*Not noted in 16 cases.

DISTINGUISHING SIMPLE AND STRANGULATED OBSTRUCTIONS

Much emphasis has been placed upon the value of certain diagnostic criteria in the differential diagnosis of simple and strangulated intestinal obstruction. Just how reliable are these so-called "signs of strangulation"?

The incidence of these various signs in the two varieties of obstruction in the present series is shown in Chart 2. Leucocyte counts were done in 373 (90.5 per cent) of the 412 cases; and in 189 (50.6 per cent) the count exceeded 10,000. Leucocytosis was present in 44.4 per cent of the cases of simple obstruction, and in 50 per cent of those with strangulated obstruction. Of the patients who died of strangulated obstruction 60.8 per cent had a normal leucocyte count.

Only 22.7 per cent of patients with strangulated obstruction had a temperature elevation to 100 degrees F. or more, and the corresponding figure for the simple obstruction group was 16 per cent.

Tachycardia, defined in this report as a pulse rate exceeding 100, was present in only 22.7 per cent of the patients with strangulation, and in 14.8 per cent of those with simple obstruction.

Abdominal or pelvic tenderness was present in 306 (74.2 per cent) of the cases. It is noteworthy that 72.2 per cent of the patients with simple obstruction exhibited tenderness. In the cases of simple obstruction due to the attachment of an adhesive band to the anterior abdominal wall, point tenderness at that site was almost invariably present. Tenderness was frequently elicited by vaginal or

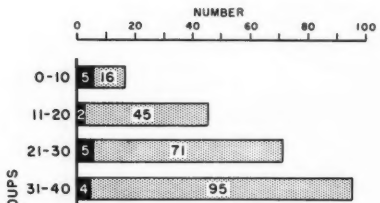

Chart 1. Distribution and mortality by age. Patients over 50 years of age comprise 26 per cent of the material and 51 per cent of the deaths. The death rate of patients 50 years of age and younger is 7.8 per cent; above 50 years it is 23.3 per cent. In 2 nonfatal cases the age is not recorded.

rectal examination in the presence of simple obstruction due to the adherence of a loop of small bowel in the depths of the pelvis. Furthermore, pelvic or abdominal tenderness was usual in those instances of simple obstruction in which increased intraluminal pressure had resulted in the transudation of clear straw-colored fluid into the peritoneal cavity. So the belief that the presence of tenderness in mechanical small bowel obstruction practically always means strangulation seems to be an erroneous one. Almost ¾ of the patients in this series exhibited tenderness, but less than ¼ of them had strangulation. Almost 20 per cent (18.2) of the patients with strangulation did not exhibit tenderness.

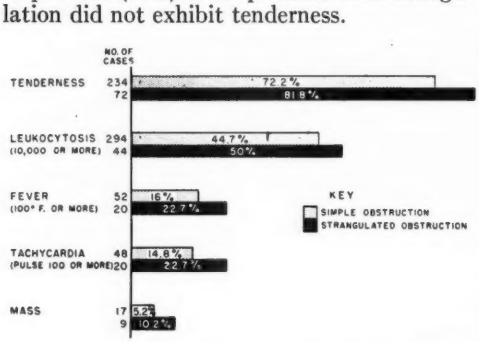

Chart 2. The relative incidence of the so-called "signs of strangulation" in simple and strangulated obstructions.

An abdominal or pelvic mass was palpable in 6.3 per cent of all cases; 10.2 per cent of the strangulated group and 5.2 per cent of those with simple obstruction.

It must be admitted that it was only the occasional patient with strangulated obstruction who failed to exhibit at least one of the so-called "signs of strangulation"; but the same may be said of simple obstruction. Only 6.8 per cent of the patients with strangulation failed to exhibit either tenderness, fever, leucocytosis, tachycardia, or a palpable mass; while in the group with simple obstruction all of these signs were absent in 12.3 per cent.

TREATMENT

The various types of therapy employed in this series of 412 cases are indicated in Chart 3. Nonoperative tube decompression (usually with the Miller-Abbott tube) was the sole method of treatment in 115 (27.8 per cent) of the cases. Operation without adjunctive intubation with the Miller-Abbott or Levin tube was performed in 35 cases (8.7 per cent). In 254 (61.6 per cent) of the cases operation was performed after varying periods of tube decompression. Of the 8 patients who received no active treatment for their obstruction, 1 was moribund on admission, 1 died on the medical service with the diagnosis being made by postmortem examination, and 6 experienced spontaneous relief of the obstruction.

The mortality in relation to the types of therapy is shown in Chart 4. The lowest mortality rate (5.7 per cent) occurred in the group of cases treated by operation alone. Treatment by intubation alone resulted in a mortality rate of 6.9 per cent. In the much larger group managed by a combination of tube decompression and operation the mortality rate was 14.6 per cent. Forty per cent of the patients in this third group had been treated by suction for more than 24 hours before being operated upon. Of the 8 patients who received no active treatment, 2 died.

RECENT VERSUS OLD ADHESIONS

The vast majority of patients with obstruction by a subacute inflammatory process due either to recent infective peritonitis or to recent surgical invasion of the peritoneum can

be safely and effectively treated by nonoperative measures. In most instances suction drainage through the Miller-Abbott tube and rest of the intestine will permit the resolution of the inflammatory process with release of fixation, diminution of edema of the bowel wall and spontaneous re-establishment of intestinal continuity. Even in this group, however, conservative therapy must be employed with great caution, and unless evidence of recovery is prompt and unequivocal operation is in order.

There were 57 patients in the present series who had obstructions caused by fresh or recent adhesions, and 10 (17.5 per cent) of them died. In too many instances treatment consisted of protracted intubation, and finally operation performed upon a prostrate, gravely ill patient. This plan of therapy was in part based on the optimistic assumption that in obstruction due to recent adhesions the danger of necrosis was minimal. Actually the incidence of strangulation in this group was 10.5 per cent. It is so easy to overextend the indications for conservatism in these cases. The surgeon must not permit his interpretation of the clinical and roentgenographic findings to be influenced by the consideration of normal postoperative ileus, nor by reluctance to submit the patient to another operation.

THE ABUSE OF TUBE DECOMPRESSION

A primary objective in a study such as this should be the improvement upon previous results by the utilization of knowledge gained from an objective analysis of past mistakes. From a review of the charts in these 412 cases of acute adhesive ileus it was apparent that errors in diagnosis were few. The major mistakes were: (1) failure to differentiate between simple and strangulated obstructions, (2) the abuse of tube decompression, and (3) failure to administer blood and plasma in adequate amounts.

TABLE II.—CLASSIFICATION OF CASES OF ACUTE ADHESIVE ILEUS IN WHICH TUBE DECOMPRESSION WAS ABUSED

Group	No. of cases	Died	Mortality per cent
I—Treatment by tube decompression for at least 12 hours; then strangulated obstruction found at operation*	43	11	25.5
II—Treatment by tube decompression alone; and strangulated obstruction found at autopsy*	3	3	100.0
III—Patient initially in good condition. Treated by prolonged tube decompression with marked deterioration. Finally operated on for simple obstruction, and died of operation.	6	6	100.0
Total	52	20	38.4

*Does not include patients who at the beginning of treatment were considered too ill to tolerate operation.

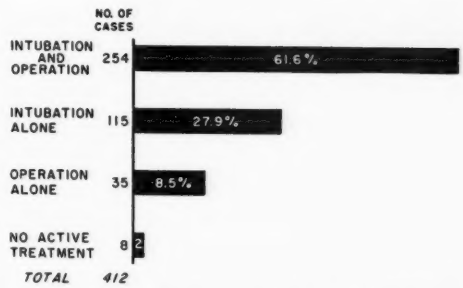

Chart 3. Types of therapy employed in the management of 412 cases of acute intestinal obstruction due to adhesions.

The question of where lies the dividing line between the use and abuse of tube decompression cannot be answered in a manner which will be acceptable to all surgeons. The cases in which it was believed that intestinal intubation was improperly used were classified as follows (Table II):

Group I. Patients treated by tube decompression for at least 12 hours, then operated upon and found to have strangulated obstruction. By definition these patients either had strangulation at the time of admission or de-

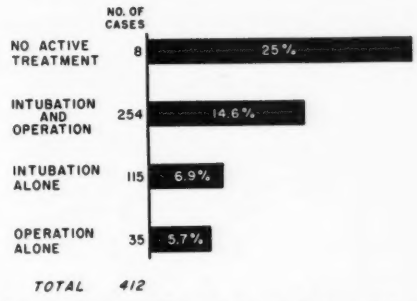

Chart 4. The mortality in relation to the type of therapy employed in the management of acute adhesive ileus in the author's series.

veloped it during the course of nonoperative treatment. This is not to deny that in most cases it is wise to institute suction and defer operation until fluid and electrolyte replacement has been effected, but it is suggested that this can usually be accomplished within less than 6 hours. In the present series 143 patients were operated upon after at least 12 hours of tube decompression; 43 (30 per cent) of them had strangulated obstruction, and 11 (25.5 per cent) of these 43 patients died.

Group II. Patients treated by tube decompression alone, and strangulated obstruction found at autopsy. There were 3 patients in this group. Excluded were 2 patients strongly suspected of having died of gangrene, perforation, and peritonitis without autopsy confirmation, and 2 others who were moribund on admission.

Group III. Patients initially in good condition, treated by prolonged intestinal intubation with marked deterioration, and finally succumbing to operation for simple obstruction. There were 6 cases in this category. In each instance the record clearly indicated that the patient's condition was considered good when suction was instituted, and that operation was resorted to after he had grown seriously ill during the course of prolonged treatment by intestinal intubation.

It is to be emphasized that neither group I, II, nor III includes patients who at the beginning of treatment were considered too ill to tolerate operation.

Thus, tube decompression was employed either as definitive or adjunctive therapy in 369 cases; and it was abused in 52 (14 per cent) of them. But the important fact is that abuse of the tube was attended by a mortality of almost 40 per cent.

SUMMARY AND CONCLUSIONS

The concept that acute intestinal obstruction due to adhesions can be safely and effectively treated by nonoperative tube decompression presupposes the existence of absolute diagnostic criteria for differentiating simple and strangulated obstructions.

An analysis of 412 cases of acute adhesive ileus indicates that the absence or presence of fever, tachycardia, leucocytosis, a palpable mass, and peritoneal irritation does not suffice to differentiate these two varieties of obstruction.

Acute intestinal obstruction due to old adhesions should be treated by early operation. The preoperative preparation of the patient by suction applied to a long intestinal decompression tube, and the correction of fluid, electrolyte, and blood volume deficits can usually be effected in a period of less than 6 hours.

Intestinal obstruction due to recent adhesions will usually respond to suction, but conservative therapy must be employed with great caution, and, unless evidence of recovery is prompt and unequivocal, operation is in order.

The mortality rate in this series of 412 cases of acute adhesive ileus was 11.8 per cent. In the 52 cases in which tube decompression was abused, the mortality rate was 38.4 per cent.

PULMONARY FUNCTION BEFORE AND AT INTERVALS AFTER SURGICAL DECORTICATION OF THE LUNG

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SURGICAL decortication of the lung has a dual objective. First, and most important, it has been shown to be an effective means of obliterating an infected or potentially infected pleural space. Secondly, our studies show that pulmonary function is improved in the majority of cases.

The very nature of the procedure suggests that, if successful, it should be followed by some improvement of pulmonary function. The compressed or incarcerated lung is released by the operation much as the constricted heart is freed for action by the removal of its limiting corset of thickened pericardium. Improvement of pulmonary function certainly enhances the attractiveness of the operation, even though it may not constitute the primary indication for its performance. Waterman and Domm have pointed out that alternative methods for obliteration of pleural space involve further deterioration rather than restoration of function. "False re-expansion" alters anatomical relationships by mediastinal shift with resulting overdistention of the opposite lung. Thoracoplasty and Schede operations destroy portions of the rib cage with further compression of the underlying lung. They may also diminish the full range of motion of the opposite hemithorax. The functional aspects of decortication should be judged not only from the standpoint of maintaining or improving what function exists at the time of operation, but from the standpoint of preventing further damage which might become a very real and disabling problem.

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Published data indicate that a definite improvement in pulmonary function often follows the operation when performed for unresolved hemothorax.

Wright and associates have reported elaborate preoperative and postoperative studies of one patient with hemothorax and postoperative observations of another (17). Preoperative respiratory deficiency was shown by marked diminution of maximum breathing capacity and vital capacity and some reduction of total lung volume. Bronchospirometry demonstrated that the abnormal findings were due to lack of participation of the involved lung. Exercise tolerance was severely limited by dyspnea. Studies 34 days after decortication showed more nearly normal values and even greater improvement was noted 7 months later. The second case, seen 40 days after surgery, showed almost normal overall function, but bronchospirometry indicated continued impairment of the involved side.

Carroll and associates studied 3 similar cases. Preoperative data were not available but it is likely that these patients had suffered severe impairment of function as had the case reported by Wright. Six months after operation findings were essentially normal. All of these patients with hemothorax underwent decortication within 7 weeks after the pleural accident.

Forsee, Kylar, and Blake reported the results of preoperative and postoperative maximum breathing capacities and bronchospirometries in 19 patients with traumatic hemothorax. The majority showed improvement following decortication. The time relationships of function studies to surgery were not stated and the clinical and operative details which might account for the variability of the observed results were not given.

When decortication was carried out in the presence of pleural or parenchymal tuberculosis the functional end results were less consistent. Because of this variability it would be essential to have both preoperative and postoperative data to evaluate the changes brought about by operation. On the whole, this group showed less return of function than was seen after decortication for hemothorax.

Gordon and Welles reported satisfactory obliteration of the pleural space in 9 patients with pleural tuberculosis. Complete studies of pulmonary function before and after operation were given in 4 cases of re-expansion. Little or no improvement was shown. It should be noted that 3 of these patients had been subjected to thoracoplasty before decortication. Decortication could hardly be expected to bring about optimal improvement.

One patient with advanced pulmonary tuberculosis, complicated by unexpandable pneumothorax and tuberculous empyema, was studied before and after decortication by Wright and associates (17). The maximum breathing capacity was unchanged, but there was an improvement in total lung volume and exercise was better tolerated. Some increase in function of the side operated upon was demonstrated by bronchospirometry. None of the changes were as striking as those commonly seen after operation for hemothorax. Arterial hypoxia was found following re-expansion, an abnormality not observed preoperatively. The authors attributed this to pulmonary arterial perfusion of poorly ventilated areas of the lung. That this case must have been rather unusual is indicated by the normal blood oxygen values found by Carroll and associates in postoperative studies of 5 patients with tuberculous pleural disease. These authors too found that lungs functioned less well following decortication in the presence of tuberculosis than after decortication for hemothorax. The exact effect of the operations could not be determined as preoperative studies were performed in only 1 case.

The literature thus yields only 13 instances of decortication in the presence of tuberculous disease studied from the standpoint of pulmonary function. Only 6 of these were observed both before and after operation. The variation in type of disease, operative technique, and timing of studies makes it difficult to form a clear picture of the functional outcome of the operation. Maier has emphasized that much more information about function of decorticated lung is needed, particularly on the effect of longstanding intrapulmonary disease and duration of collapse.

CLINICAL MATERIAL

The patients studied were unselected in the sense that they were the first 14 referred to the laboratory both before and after decortication. Two nontuberculous patients were included. One had a traumatic hemothorax complicated by Clostridium welchii empyema and the other a Staphylococcus aureus empyema and severe diabetes. All other patients suffered from tuberculosis with pleural complications (Table I).

CLINICAL RESULTS

More conservative procedures such as aspiration of fluid, oxygen lavage, open and closed drainage, or instillation of streptokinase-streptodornase had been ineffective in obliterating the pleural space in all patients before decortication was performed. The pleural disease was considered severely disabling or life-threatening in 11 of the 14 cases.

Decortication alone was effective treatment in 9 patients. The other 5 required additional measures to bring about a satisfactory result. R.M. showed excellent re-expansion but was left with a bronchopleural fistula which was subsequently closed by a two rib Schede operation. D.S. required a 2 rib thoracoplasty to fill a residual apical space. Fluid persisted after operation in the pleural space of T.S. and was gradually replaced over a period of months by fibrothorax. An 8 rib thoracoplasty controlled the empyema of L.R. after decortication had failed. Finally, the persistent empyema and bronchopleural fistula of G.H. was corrected by thoracoplasty.

Patients were followed for periods varying from 6 months to 3 years after decortication. All are living and none have persistent pleural space or empyema. Only 1 patient (T.S.) is still hospitalized because of the subsequent development of extensive lymph glandular

TABLE I.—CLINICAL DATA OF 14 PATIENTS SUBJECTED TO PULMONARY DECORTICATION

Case Sex Age	Height in cm.	Body surface in m^2	Parenchymal disease		Side operated upon	Collapse		Fluid			Extent of decortication	Per cent collapse estimated from roentgenograms	
			Right	Left		Cause	Duration, mos.	Duration, mos.	Type	Bacteriology		Preop.	Postop.
R.W. M 30	183	1.99	o	o	Rt.	Traumatic hemothorax	4	4	Blood pus	Cl. welchii	Complete	50	o
R.M. M 22	171	1.68	o	o	Lft.	Staphylococcus empyema	2	2	Pus	Staph. aureus	Visceral	80	10
D.S. M 32	175	1.66	Minimal	o	Rt.	Therapeutic pneumothorax	13	9	Clear	Neg.	Complete	75	20
C.C. F 31	165	1.48	Minimal	o	Rt.	Therapeutic pneumothorax	72	42	Clear	Neg.	Complete	100	o
E.G. F 40	175	1.55	Minimal	o	Rt.	Therapeutic pneumothorax	78	20	Pus	Neg.	Complete	90	o
W.B. M 32	188	2.15	Minimal	o	Rt.	Therapeutic pneumothorax	48	42	Cloudy	Myco. tbc.	Complete	60	10
R.G. M 32	170	1.77	Prob. min.	o	Rt.	Persistent effusion	6	6	Clear	Neg.	Complete	75	5
T.S. M 58	179	2.00	Prob. min.	o	Rt.	Empyema	12	12	Pus	Myco. tbc.	Complete	90	50
L.L. M 21	170	1.64	Mod. adv.	o	Rt.	Therapeutic pneumothorax	7	1	Clear	Neg.	Complete	85	5
L.R. M 45	180	1.84	Prob. mod. adv.	Minimal	Rt.	Empyema	72	72	Cloudy	Myco. tbc.	Unsatisfactory	50	50
G.M. M 38	178	1.60	Mod. adv.	Far adv.	Rt.	Therapeutic pneumothorax	54	14	Clear	Neg.	Unsatisfactory	80	o
G.H. M 43	183	1.89	Mod. adv.	Minimal	Rt.	Empyema bronchopleural fistula	24	24	Cloudy	Myco. tbc.	Unsatisfactory	20	20
M.W. M 30	173	1.70	Mod. adv.	o	Rt.	Therap. pneumothorax, thoracoplasty	12	10	Cloudy	Myco. tbc.	Visceral	90	75
F.G. M 47	170	1.92	Far. adv.	Mod. adv.	Rt.	Therap. pneumothorax, thoracoplasty	36	16	Pus	Myco. tbc.	Visceral	75	50

tuberculosis. His pleural disease was brought under control by decortication. The activities of 1 patient (G.M.) are limited by cough and some dyspnea following "false re-expansion" and performance of a contralateral thoracoplasty. The remaining 12 live normal or only moderately restricted lives.

METHODS

The methods of pulmonary functional evaluation used have been previously described in detail (8).

The maximum breathing capacity was collected for 30 seconds with a high velocity respiratory valve and Douglas bag. The volume was measured in a Tissot spirometer, corrected to body temperature, ambient pressure and saturated with water vapor (BTPS), and reported in liters per minute. The predicted normal maximum breathing capacities and vital capacities were calculated from the linear regression equations of Baldwin and associates. The air velocity index was obtained from the formula:

$$\frac{\text{per cent of predicted maximum breathing capacity}}{\text{per cent of predicted vital capacity}}.$$

In normal volunteers this index is 1.0 ± 0.1. Higher indices are indicative of chronic restrictive ventilatory insufficiency while lower indices point to obstructive defect (7).

The walking ventilation was collected with valve and bag during the second, third, and fourth minutes of a level walk at the rate of 180 feet per minute, corrected to BTPS and reported in liters per minute. This walking ventilation is 10 liters $\pm$ 2 liters per minute, per square meter of body surface in normal volunteers and in most patients with pulmonary disease. The walking index was calculated from the formula:

$$\frac{\text{walking ventilation in liters per minute}}{\text{maximum breathing capacity in liters per min.}} \times 100.$$

The result expresses the percentage of the maximum effort a patient requires for this mild form of exercise (15).

Bronchospirometry was performed with a flexible double lumen catheter and closed circuit recording spirometers. The Gebauer catheter, as modified by Wright (18), was used for the first 2 years of the study while the Carlens tube was used the last year. During the procedure patients usually breathed oxygen rich mixtures. Recently, ambient air recording bronchospirometry was used (9). The correct position of the tube was checked by fluoroscopy and spot films. Two tracings with the tube in slightly different positions were made. In the illustrations the upper tracing always depicts the spirogram of the right lung.

The ventilatory equivalents were calculated for each side according to the formula:

$$\frac{\text{minute ventilation in liters}}{\text{minute oxygen uptake in c.c.}} \times 100 \text{ (1)}.$$

These equivalents represented the number of liters of ventilation required for uptake of 100 cubic centimeters of oxygen.

These studies were carried out in all patients both before and after operation. Other data, obtained only before or only after operation, included arterial oxygen content and saturation, residual volume, pulmonary mixing indices, and timed capacity studies. Because we were chiefly interested in establishing pulmonary functional patterns before and after operation these were not reported. Fluoroscopy was part of the routine functional evaluation and was carried out as suggested by Warring.

RESULTS OF PULMONARY FUNCTION STUDIES

In Table I the 14 patients were arranged in a sequence determined by the extent of pulmonary parenchymal infection which had existed at any time prior to the operation. Standards of the National Tuberculosis Association for minimal, moderately advanced, and far advanced disease were used in this classification. When the functional data were tabulated in the same order it was found that the postoperative improvement correlated closely with the severity of pre-existing parenchymal disease, so closely in fact, that the evaluation of results was facilitated by dividing the patients into three groups. Group I consisted of 8 patients with no parenchymal disease or only minimal involvement. Group II was comprised of 4 patients with moderately advanced or far advanced disease. In 2 patients, re-expansion of the decorticated lung was limited by previous extensive thoracoplasty, and the results were not strictly comparable with those obtained in patients with an intact rib cage. The patients with thoracoplasty were therefore considered separately as group III.

GROUP I: PATIENTS WITH NO OR MINIMAL PARENCHYMAL DISEASE

Preoperative studies. The average maximum breathing capacity was reduced to 68 per cent and the average vital capacity to 65 per cent of the predicted normal (Table II). This reduction of overall function to about two thirds of predicted suggested that the affected lung contributed little to ventilatory activity. The almost equal reduction of maximum breathing capacity and vital capacity indicated that the ventilatory defect was primarily of the restrictive, as opposed to the obstructive, type. The speed of the expiratory airstream expressed by an air velocity index of 1.09 was normal. No hyperventilation was apparent during the standard walking exer-

TABLE II.—PULMONARY FUNCTION STUDIES IN PATIENTS WITH NO OR MINIMAL PARENCHYMAL DISEASE (GROUP I)

Case	Op. side	Timing of studies	Overall Ventilation Studies							Bronchospirometry							
			Max. breath. cap.		Vital capac.		Air veloc. index % MBC / %VC	Walking test		Oxygen uptake per cent of total		Resting Ventil., per cent of total		Vital capacity, per cent of total		Ventilation equivalent, L./100 c.c.	
			Liters per minute	Per cent of predict.	c.c.	Per cent of predict.		Liters per minute	Walk. index	Op. side	Well side	Op. side	Well side	Op. side	Well side	Op. side	Well side
W.	Rt.	1 day preop.	116	82	3210	72	1.14	20	17	23	77	35	65	19	81	2.5	1.5
		2 weeks postop.	128	91	3270	73	1.24	—	16	31	69	48	52	23	77	5.0	2.4
		6 months postop.	135	96	4720	106	0.90	—	15	40	60	67	33	51	49	2.8	1.3
M.	Lft.	4 days preop.	72	57	2100	49	1.17	14	19	7	93	7	93	7	93	2.8	2.8
		8 months postop.	112	88	3200	74	1.19	—	13	27	73	35	65	36	64	3.3	2.2
		2½ years postop.	123	97	3390	79	1.23	—	11	—	—	—	—	—	—	—	—
S.	Rt.	1 week preop.	68	59	2700	64	0.92	13	19	22	78	33	67	19	81	3.3	1.9
		2 weeks postop.	95	82	3000	71	1.15	—	14	28	72	39	61	27	72	3.8	2.3
		2 mos.+2 r. thpl.	95	82	2800	65	1.25	—	14	25	75	43	57	22	78	5.6	2.5
C.	Rt.	1 week preop.	75	90	2200	73	1.24	13	17	5	95	28	72	16	84	12.0	1.7
		2 weeks postop.	75	90	1700	52	1.73	—	17	28	72	54	46	37	63	5.6	1.9
		7 months postop.	108	130	2520	82	1.58	—	12	45	55	61	39	46	54	3.9	2.0
		3 years postop.	106	128	2450	81	1.58	—	12	—	—	—	—	—	—	—	—
G.	Rt.	3 days preop.	54	56	1650	53	1.06	16	30	8	92	23	77	10	90	8.1	2.3
		7 months postop.	62	65	2200	70	0.93	—	26	53	47	45	55	51	49	1.6	2.2
		2½ years postop.	69	72	2450	78	0.92	—	23	—	—	—	—	—	—	—	—
W.B.	Rt.	5 days preop.	52	35	3600	80	0.44	14	27	32	68	61	39	40	60	4.4	1.2
		2 weeks postop.	122	81	3600	80	1.01	—	11	33	67	56	44	29	71	6.3	2.5
		6 months postop.	126	84	3700	82	1.03	—	11	—	—	—	—	—	—	—	—
R.G.	Rt.	1 week preop.	110	89	2930	72	1.24	24	22	6	94	44	56	8	92	14.4	1.2
		7 months postop.	167	136	4250	104	1.31	—	14	45	55	62	38	45	55	3.4	1.7
T.S.	Rt.	2 weeks preop.	83	74	2030	54	1.37	29	35	10	90	32	68	26	74	6.7	1.6
		5 weeks postop.	102	91	2400	63	1.45	—	28	20	80	67	33	—	—	12.0	1.5
		11 months postop.	105	94	2700	71	1.32	—	28	39	61	56	44	43	57	6.7	3.3
Mean		Preoperative	79	68	2550	65	1.07	18	23	14	86	33	67	18	83	6.8	1.8
		Early postop.	111	93	2930	75	1.25	—	16	—	—	—	—	—	—	—	—
		Late postoperative	116	99	3310	84	1.19	—	16	38	62	53	47	40	60	4.2	2.2

cise test. Because of the lowered maximum breathing capacity the breathing reserve was reduced and the walking index was elevated to 23 per cent.

Bronchospirometric observations confirmed the impressions gained by the overall function studies. The ventilatory insufficiency appeared to be almost entirely due to extensive collapse of the involved lung. In mean values, the affected lung was responsible for 14 per cent of the total oxygen uptake, 33 per cent of the total ventilation, and 18 per cent of the total vital capacity. The discrepancy between the share of ventilation and oxygen uptake borne by the diseased lung was reflected by the two ventilatory equivalents. The affected lung moved 6.8 liters of the respired gas for absorption of 100 cubic centimeters of oxygen while the opposite lung moved only 1.8 liters.

Early postoperative evaluation. In most instances, tests were performed 2 weeks after operation. Occasionally, as much as 8 months

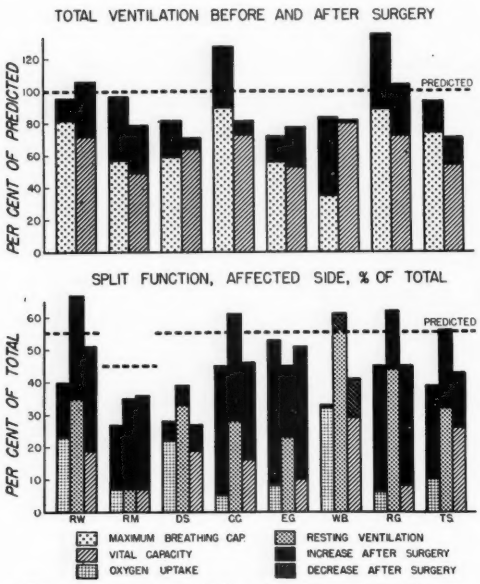


Fig. 1. Overall ventilation (maximum breathing capacity and vital capacity as per cent of predicted) and participation in oxygen uptake, ventilation, and vital capacity by the involved lung (bronchospirometry) before and late after decortication of 8 patients with no or minimal parenchymal disease (group I).

had elapsed before the first postoperative study. The inclusion of the few late studies resulted in somewhat higher mean values than were observed in most patients in the immediate postoperative period. The maximum breathing capacity was 111 liters per minute, a 41 per cent increase over the preoperative performance. The mean vital capacity was 15 per cent higher. The larger increase of maximum breathing capacity resulted in an elevation of the air velocity index (Table II). Bronchospirometric studies were seldom performed so soon after operation.

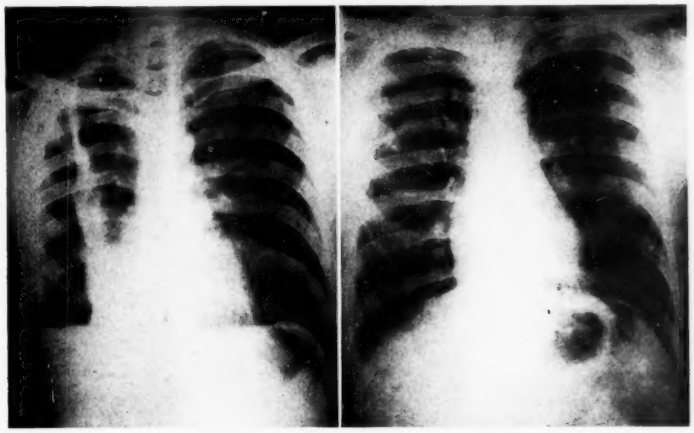
Late postoperative studies. The tests summarized as "late" were the most recent available and were obtained up to 3 years after decortication. Although most patients showed continued improvement during the first year, it did not seem likely that inclusion of 2 patients studied less than a year after operation altered the late results greatly. These 2 patients happened to have shown prompt reexpansion and early improvement of function.

The average maximum breathing capacity had increased further to 47 per cent above the preoperative figure and the vital capacity had increased by 31 per cent. The walking index had further diminished to 16 per cent.

Late bronchospirometric studies revealed the average lung operated upon to be responsible for 38 per cent of the total oxygen uptake which was 172 per cent more than the preoperative participation. Ventilation was 53 per cent of total, a figure well within normal predicted limits and representing a 62 per cent increase. The vital capacity of the affected side was now 40 per cent of total vital capacity, a 136 per cent gain. The mean ventilatory equivalent was 3.5 liters per 100 cubic centimeters on the affected side and 2.7 liters per 100 cubic centimeters on the opposite side (Table II). Figure 1 shows both the preoperative and the late ventilation studies and bronchospirometries of patients in this group. The good functional outcome, apparent from the average figures, was the result of a fairly uniform improvement in every single instance. Furthermore, there was a good correlation in each patient between the degree of functional improvement as expressed by maximum breathing capacity and vital capacity and by increase of function of the involved lung.

Comment. Individual variations in this group of patients with little or no parenchymal disease were small. The preoperative defect of overall function was marked and tended to follow the same pattern in each with almost equal reduction of static vital capacity and dynamic maximum breathing capacity values. All showed a return to near normal function after operation.

Bronchospirometry showed a striking abnormality in the distribution of function between the two lungs in all but 1 case (W.B.). In this patient the preoperative bronchospirometry, performed at another institution, suggested that the involved right lung was responsible for a share of the function entirely out of proportion to the roentgenographic picture. This unusual spirogram may have been due to accidental and unrecognized occlusion of the left upper lobe orifice by the catheter balloon giving an erroneous impression of the distribution of function between



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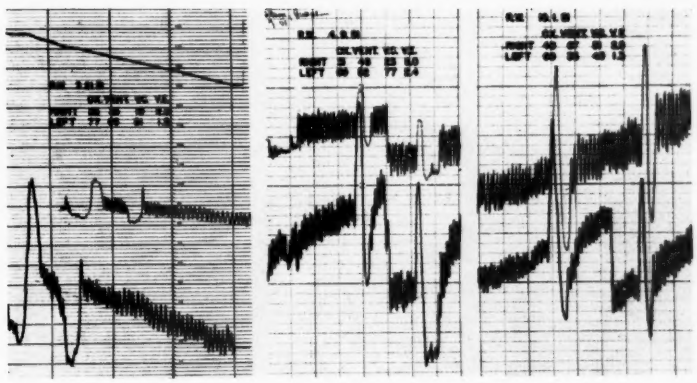

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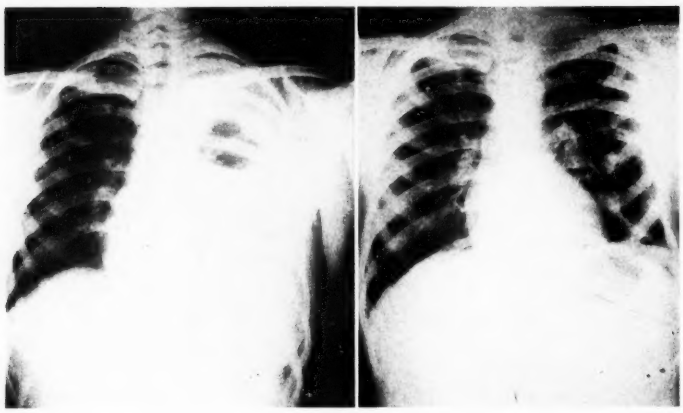
Fig. 2. Patient R.W. (group I), 30 year old male. Hemopneumothorax due to stab wound, complicated by Clostridium welchii empyema. Re-expansion was complete 6 months after decortication. The first bronchospirogram, before operation, showed severe impairment of oxygen uptake and vital capacity and lesser impairment of ventilation on the right side. The second tracing, 2 weeks after operation, suggests slight improvement. The last tracing, 6 months after decortication, shows normal distribution of ventilation and vital capacity and near normal oxygen uptake on the right. The first tracing, unlike all others, reads from right to left. In this and all subsequent illustrations the *upper* tracing represents the spirogram of the *right* lung.

the two lungs. Postoperative bronchospirometry was performed in this patient only 2 weeks after operation and it seemed likely that the apparent loss of function was due to timing of the postoperative bronchospirometry and/or a technical error in the performance of preoperative study.

Oxygen uptake was reduced to the greatest degree in the collapsed lung and returned slowly and incompletely after re-expansion. This was in contrast to resting ventilation which showed the least decrease in the presence of collapse and the greatest gain after operation. Indeed, after decortication, ventilation was greater than predicted in 3 cases.

Three patients of this group were chosen for illustration because they were representative of the improvement in function achieved in



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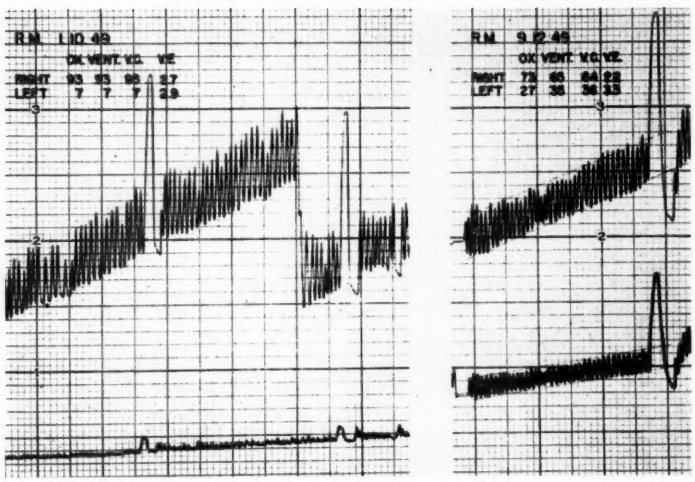

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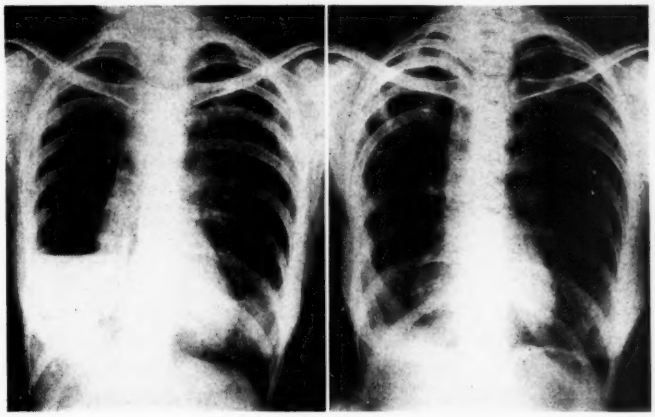
Fig. 3. Patient R.M. (group I), 21 year old male diabetic. Collapse of the left lung due to Staphylococcus aureus empyema. The second chest film, taken 8 months later, shows complete re-expansion. A small residual pocket with bronchopleural fistula was closed by resection of small segments of eighth and ninth ribs. The second bronchospirogram, 8 months after operation, reveals close to normal participation of the left lung.

group I and because they represent pleural disease of three different types: traumatic (Patient R.W., Fig. 2), pyogenic (Patient R.M., Fig. 3), and tuberculous (E.G., Fig. 4).

GROUP II: PATIENTS WITH MODERATELY OR FAR ADVANCED PARENCHYMAL DISEASE

Preoperative studies. In this group of 4 patients the average maximum breathing capacity was reduced to 80 per cent and the vital capacity to 64 per cent of the predicted normal. The resultant high air velocity index was 1.26, a common finding in patients with chronic restrictive disease with considerable reduction of functioning lung parenchyma. Ventilation during the standard walking exercise was 17 liters per minute, exactly as predicted for the group. Reduction of maximum



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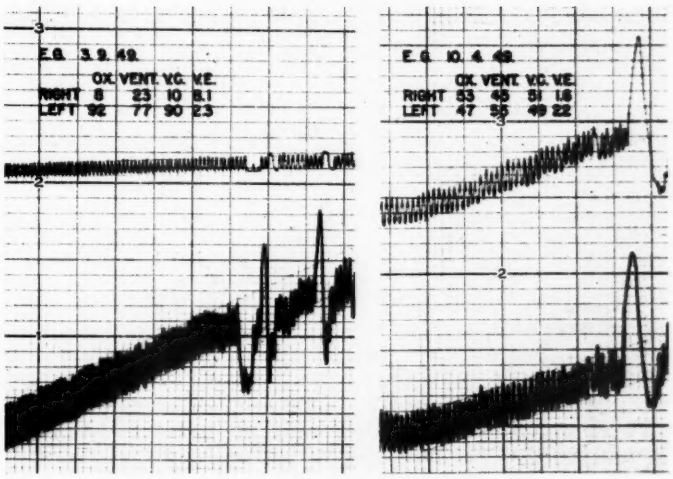

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Fig. 4. Patient E.G. (group I), 40 year old female. Minimal pulmonary tuberculosis was treated for 78 months by artificial pneumothorax. The lung failed to re-expand when treatment was discontinued as shown by the first chest film. Prompt and complete re-expansion after decortication is shown by the film on the right taken 7 months after operation. Bronchospirograms, obtained just before and 7 months after decortication, gave evidence of return to normal participation by the initially functionless right lung.

breathing capacity caused a slight elevation of walking index to 18 per cent (Table III).

Early postoperative studies. Tests of overall function were performed in all cases between 2 and 3 weeks after operation. The average maximum breathing capacity was 15 per cent less and the vital capacity 14 per cent less than before operation. The diminution of these values was reflected by a rise of walking index from 18 to 27. The loss of function at this time was due, at least in part, to pain at the site of operation interfering with examinations requiring maximal voluntary efforts (Table III).

TABLE III.—PULMONARY FUNCTION STUDIES IN PATIENTS WITH ADVANCED PARENCHYMAL DISEASE (GROUP II)

Case	Op. side	Timing of studies	Overall Ventilation Studies							Bronchospirometry							
			Max. breath. cap.		Vital Capac.		Air veloc. index % MBC	Walking test		Oxygen uptake, per cent of total		Resting ventil., per cent of total		Vital capacity, per cent of total		Ventilation equivalent, L./100 c.c.	
			Liters per minute	Per cent of predict.	c.c.	Per cent of predict.	% VC	Liters per minute	Walk. index	Op. side	Well side	Op. side	Well side	Op. side	Well side	Op. side	Well side
L.L.	Rt.	1 day preop.	88	69	2300	54	1.28	16	18	17	83	28	72	37	63	6.8	2.5
		3 weeks postop.	98	77	2500	58	1.33		16	23	77	54	46	33	67	8.9	2.3
		3 months postop.	100	79	2600	60	1.32		16	25	75	50	50	38	62	8.7	2.9
L.R.	Rt.	2 weeks preop.	97	84	2600	64	1.31	17	18	15	85	31	69	19	81	4.3	1.7
		2 weeks postop.	80	69	2200	54	1.28		21	14	86	15	85	14	86	2.3	2.1
		1 year postop.	87	75	2360	58	1.29		20	—	—	—	—	—	—	—	—
		2 yrs. and 8r. thplsty.	81	70	2190	54	1.30		21	—	—	—	—	—	—	—	—
G.M.	Rt.	7 weeks preop.	89	82	2820	68	1.21	18	20	27	73	34	66	17	83	3.4	2.4
		3 weeks postop.	56	52	2380	57	0.91		32	28	72	38	62	20	80	5.0	3.2
		2½ yrs. and 7r. thpl. opp. side	73	68	1700	42	1.62		25	33	67	36	65	26	74	3.2	2.8
G.H.	Rt.	1 day preop.	105	87	2950	71	1.22	18	17	42	58	40	60	32	68	3.1	3.3
		2 weeks postop.	90	74	2120	52	1.42		20	—	—	—	—	—	—	—	—
		3 months postop.	96	79	2390	57	1.39		19	15	85	29	71	22	78	4.3	1.9
		1 yr. and 8r. thplsty.	66	55	2160	52	1.06		27	20	80	37	63	27	73	4.3	2.6
Mean		Preoperative	95	80	2670	64	1.26	17	18	25	75	33	67	26	79	4.4	2.5
		Early postop.	81	68	2300	55	1.24		27	—	—	—	—	—	—	—	—
		Late postop.	89	75	2240	54	1.40		20	23	77	35	65	26	74	4.6	2.6

Late postoperative studies. The latest observations in this group, 3 months to 1 year after operation, showed that recovery of function had been poor. The maximum breathing capacity was still 6 per cent less and the vital capacity 16 per cent less than before operation. The breathing reserve, indicated by a mean walking index of 20 remained unchanged.

Late bronchospirometric observations demonstrated little changes in the extent of participation of the involved lung. Two patients showed slight gain in function on the side operated upon and 2 showed a slight loss. The mean share of oxygen uptake and ventilation remained virtually unchanged and the vital capacity on the side operated upon increased slightly. The ventilatory equivalent averaged 4.6 liters per 100 cubic centimeters for the involved and 2.6 liters per 100 cubic centimeters for the uninvolved side (Table III). The poor average results were due to small changes in function of individual patient. Again, patients who showed decrease of maximum breathing capacity and vital capacity were the same ones whose involved lung participated to a lesser extent in respiration after operation (Fig. 5).

Comment. The patients of group II showed less initial impairment of function than was seen in group I, even though they had greater pulmonary parenchymal damage. The better initial function was undoubtedly due to the lesser degree of collapse due to pleural disease. From the roentgenograms this initial collapse was estimated as 54 per cent for group II and 77 per cent for group I.

The late studies indicated that there had been little recovery from the reduction evident in the early postoperative period. The average overall function was less than had been found preoperatively and the contribution of the diseased lung to the total remained un-

changed. The operations were regarded as technically unsatisfactory in 3 of the 4 patients in this group.

Roentgenograms and bronchospirograms of 2 representative patients of group II are shown. One illustrated "false re-expansion" after unsatisfactory decortication (Patient G.M., Fig. 6) and the other shows the unsatisfactory results of decortication in the presence of bronchopleural fistula (Patient G.H., Fig. 7).

GROUP III: PATIENTS WITH PREVIOUS THORACOPLASTY

Early postoperative studies. The degree of collapse of the involved lung of these 2 patients was severe and the impairment of overall function was greater than that seen in the preceding groups. Maximum breathing capacity averaged 59 per cent and vital capacity 52 per cent of predicted normal. The walking index was elevated to 29 (Table IV).

Bronchospirometric studies showed a completely functionless lung in 1 patient and poor participation in the other (Table IV).

Early postoperative studies. Tests were carried out in both cases 2 weeks after operation. A further reduction of both maximum breathing capacity and vital capacity was found as was true in the early studies of patients in group II. The walking index of 31.0 was close to the dyspnea level (15).

Late postoperative studies. Two and one-half to 3 years after decortication both patients showed an overall function greater than had been observed preoperatively. Bronchospirometry showed that the functionless lung of one had resumed some respiratory activity; the involved side of the other contributed more than before operation (Table IV, Fig. 5).

Comment. The degree of collapse imposed by the thoracoplasty prevented a return of function comparable to the improvement seen in group I. Nevertheless, there was a significant increase over preoperative levels and both patients showed a final function comparable to that of patients with thoracoplasty not complicated by empyema. The uncompressed portions of the decorticated lung had apparently undergone the completest re-expansion.

Patient M.W., whose right lung had remained functionless as long as 3 months after operation, was selected for illustration (Fig. 8). He demonstrated the improvement with passing of time seen in the other groups. Correlation of roentgenograms with bronchospirograms was striking.

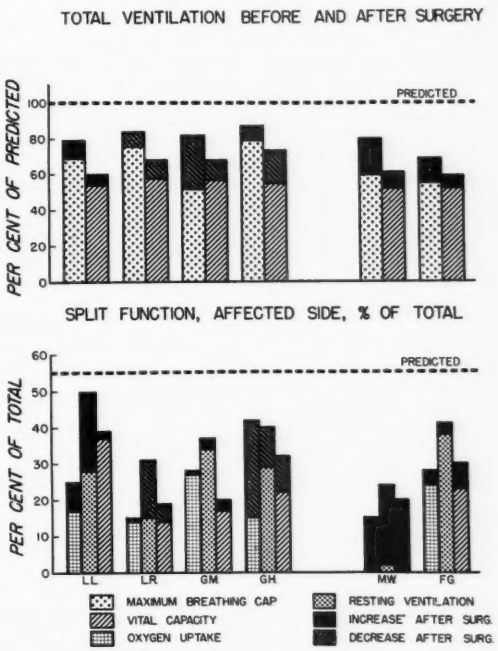

Fig. 5. Overall ventilation (maximum breathing capacity and vital capacity as per cent of predicted) and participation in oxygen consumption, ventilation and vital capacity by the involved lung (bronchospirometry) before and late after decortication of 4 patients (left) with moderately or far advanced parenchymal disease (group II) and 2 patients (right) with prior thoracoplasty (group III).

DISCUSSION

Our observations are in agreement with those of others showing that the effect of decortication on pulmonary function is highly variable. This variability is greatest when the operation is performed in the presence of pleural or parenchymal infection. A number of explanations have been suggested but, on the whole, no consistent or reliable method for predicting the functional outcome has been evolved. It seemed therefore important to correlate some of the clinical findings with the amount of functional recovery manifested.

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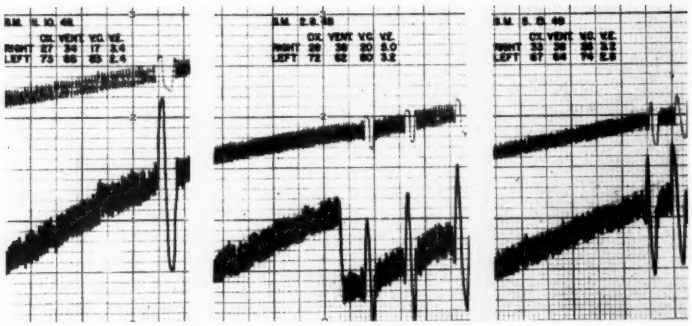

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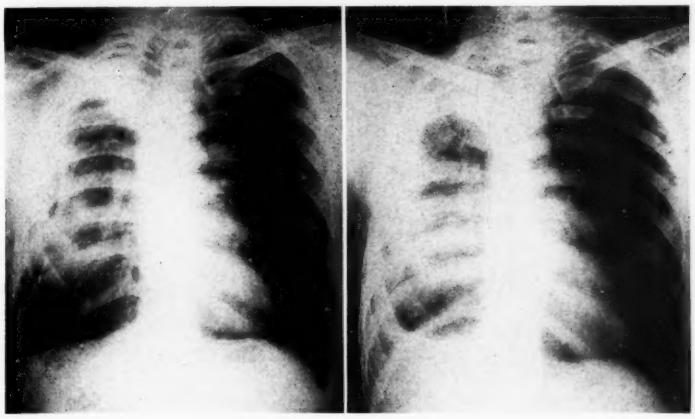
Fig. 6. Patient G.M. (group II), 38 year old male. Moderately advanced tuberculous involvement of the right lung was treated with artificial pneumothorax for 54 months. Decortication was unsatisfactory. "False re-expansion" due to mediastinal shift and distention of the opposite lung was responsible for successful obliteration of the infected space. Progressive cavernous disease on the left was treated by thoracoplasty some time after decortication on the right. Bronchospirograms showed little change 2 months after decortication (center) and the decorticated lung participated to a larger extent in the last tracing only because function on the other side had meanwhile been reduced by thoracoplasty.

The preoperative and postoperative functional data, expressed as per cent changes, were rearranged according to various clinical aspects of the cases (Figs. 9 to 11). The effect of surgical technique, the amount of re-expansion estimated from the chest roentgenogram, the duration of collapse, and the bacteriology and appearance of the pleural fluid were analyzed in this manner. The changes in differential function were not included in these charts since they paralleled the overall changes in almost every case.

Parenchymal disease and recovery of function. Allusion has already been made to this most important single factor. It appears that a good return of function may be expected if the underlying lung is not damaged and that patients with extensive pulmonary parenchymal disease show little if any recovery of function.

Decortication of the collapsed upper portion of the lung was not attempted in the patients who had previous thoracoplasty. Since this area was the principal site of parenchymal involvement the decorticated lower portions were not considered as having more than minimal disease. In Figure 9 these cases were shifted to the "none or minimal" group. This



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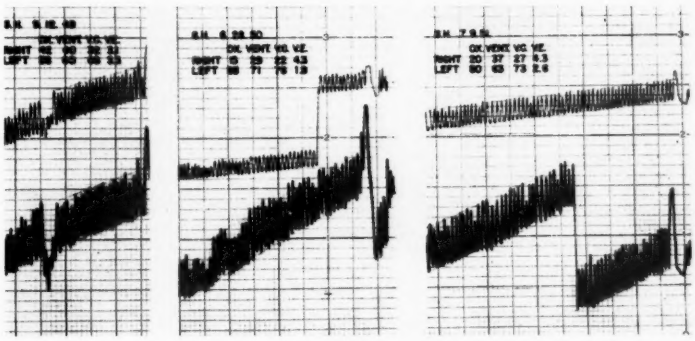

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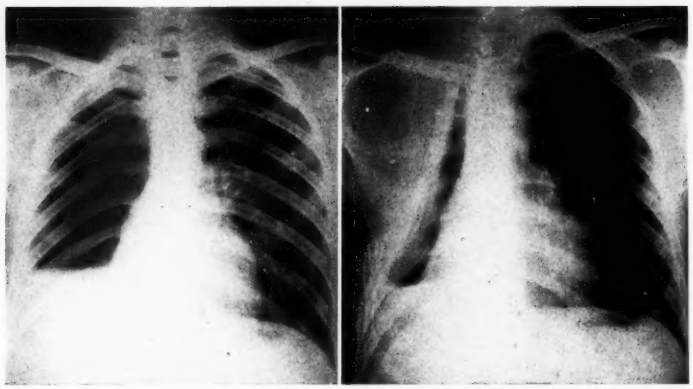
Fig. 7. Patient G.H. (group II), 43 year old male. Moderately advanced tuberculosis complicated by mixed empyema and bronchopleural fistula. There was less expansion of the right lung 2 months after decortication than prior to operation. The bronchospirogram, 2 months after operation (center) showed that respiratory participation of the affected lung was also less than before operation. Repeated bronchospirometry, 1 year after decortication, showed some increase of function in spite of an 8 rib thoracoplasty performed on that side to obliterate the infected space.

diagram, therefore, correlates the functional end results with the *amount of disease underlying the portion of lung which was decorticated.*

Relationship of operative performance on recovery of function. Surgical success in removal of the peel and the extent of decortication were designated in Table I as "complete," "visceral," or "unsatisfactory." The first category comprises those cases in whom it was planned to remove both the entire visceral and entire parietal peel. This was not always possible, but at least three-fourths of both surfaces were stripped in all these cases. In the operations referred to as "visceral" decortication no attempt was made to remove the fibrous covering of the parietes. In 3 patients the peel was so densely adherent that it was impossible to establish a plane of cleavage and only small patches could be removed by blunt, or more often sharp dissection. These operations were classified as "unsatisfactory."

The completeness of the visceral decortication depended on conditions encountered at operation. These in turn were largely determined by the amount of underlying parenchymal disease, particularly if the disease was



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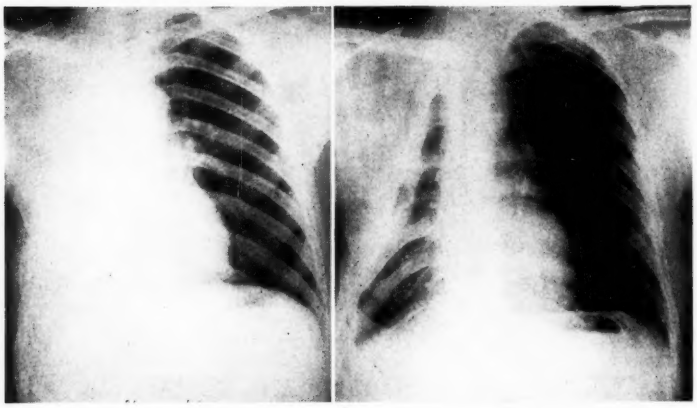

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Fig. 8. Patient M.W. (group III), 30 year old male. Moderately advanced tuberculosis was treated with artificial pneumothorax on the right for 12 months. Tuberculous empyema developed and the lung became atelectatic and failed to re-expand (first film). An attempt to close the infected space with an 8 rib thoracoplasty failed (second film). Decortication of the middle and lower lobes of the right lung brought about obliteration of the space shown by the third film 3 months after operation. The initial bronchospirogram, obtained after thoracoplasty, showed the right lung to be functionless. Decortication brought about no improvement 3 months later (center). Repeated bronchospirograms 3 years after decortication (right) showed considerable resumption of function in spite of the extensive thoracoplasty. This coincided with clearing of the lung on the last chest film.

located immediately subjacent to the pleura. All the "unsatisfactory" operations occurred in the group with more advanced parenchymal involvement. Even in the "complete" operations it was often necessary to leave patches of cortex, varying from 2 to 4 centimeters in diameter over areas of previous parenchymal disease.

It is not surprising, therefore, that the diagram relating the type of surgery to function is largely a reflection of the one relating parenchymal disease to function (Fig. 9). Whether or not the parietal peel was removed depended on the judgment of the surgeon. This was usually based on the clinical condition of the patient after removal of the visceral cortex, the length of the operation, and the ease with which the cortex separated from the chest wall. One point bears noting. It was possible to bring about a marked increase in function without removing the parietal layer. This was well illustrated by patient R.M.

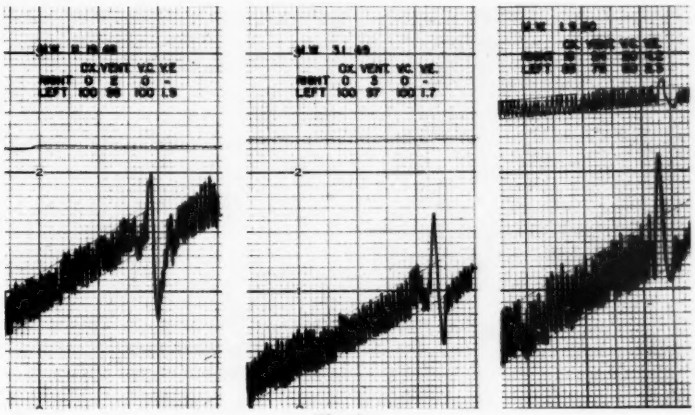

Fig. 8c.

(Legend on opposite page.)

Fig. 3, Table II) and the 2 postthoracoplasty cases (Fig. 8, Table IV).

Roentgenographic evidence of re-expansion and functional improvement. The preoperative studies demonstrated that the degree of pulmonary insufficiency correlated very well with the degree of collapse judged from the chest roentgenogram. The postoperative increase of function bore a similar close correlation to the amount of re-expansion shown by

TABLE IV.—PULMONARY FUNCTION STUDIES IN PATIENTS WITH THORACOPLASTY PRIOR TO DECORTICATION (GROUP III)

Case	Op. side	Timing of studies	Overall Ventilation Studies							Bronchospirometry							
			Max. breath. cap.		Vital Capac.		Air veloc. index % MBC	Walking test		Oxygen uptake, per cent of total		Resting ventil., per cent of total		Vital capacity, per cent of total		Ventilation equivalent, L./100 c.c.	
			Liters per minute	Per cent of predict.	c.c.	Per cent of predict.	% VC	Liters per minute	Walk. index	Op. side	Well side	Op. side	Well side	Op. side	Well side	Op. side	Well side
M.W.	Rt.	Before 8 r. thplsty.	78	65	2380	57	1.14	20	26	—	—	—	—	—	—	—	—
		3 months after typl.,3dayspreop.	71	60	2200	52	1.15	—	28	0	100	2	98	0	100	—	1.9
		2 weeks postop.	76	63	2100	50	1.26	—	26	—	—	—	—	—	—	—	—
		4 months postop.	88	73	2340	56	1.30	—	23	0	100	3	97	0	100	—	1.7
		3 years postop.	96	80	2580	61	1.31	—	21	15	85	24	76	20	80	4.2	2.3
F.G.	Rt.	Before 6 r. thplsty	47	40	2010	53	0.75	20	43	—	—	—	—	—	—	—	—
		3 months after thpl., 2 days preop.	68	57	1990	52	1.10	—	29	24	76	39	61	23	77	3.3	1.7
		2 weeks postop.	56	47	1680	44	1.07	—	36	—	—	—	—	—	—	—	—
		1 month postop.	63	53	1720	45	1.18	—	32	—	—	—	—	—	—	—	—
		4 months postop.	70	59	1800	47	1.25	20	28	27	73	41	59	30	70	3.4	1.8
		3 years postop.	82	69	2230	59	1.17	20	24	—	—	—	—	—	—	—	—
Mean		Before decortication	70	59	2095	52	1.13	20	29	12	88	21	79	12	88	—	1.8
		Early postop.	66	55	1890	47	1.17	—	31	—	—	—	—	—	—	—	—
		Late postop.	89	74	2405	60	1.24	—	23	21	79	33	67	25	75	3.8	2.1

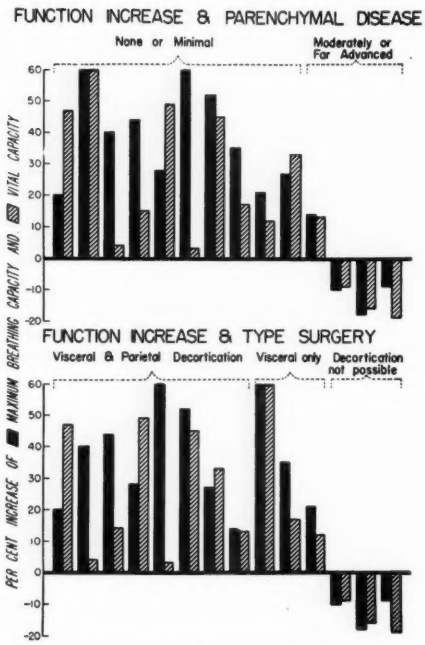
FUNCTION INCREASE & PARENCHYMAL DISEASE
None or Minimal
Moderately or Far Advanced
FUNCTION INCREASE & TYPE SURGERY
Visceral & Parietal Decortication
Visceral only Decortication not possible
PER CENT INCREASE OF MAXIMUM BREATHING CAPACITY AND VITAL CAPACITY

Fig. 9. Maximum breathing capacity and vital capacity expressed as per cent change due to decortication related to extent of tuberculous involvement (top) and related to completeness of surgical decortication (bottom).

the roentgenogram. The cases were classified according to the degree of re-expansion achieved (Fig. 10). The functional result of the operation could be estimated fairly accurately from the appearance of the postoperative roentgenogram. In general, the roentgenogram taken on deep inspiration is of little help in evaluating pulmonary function. Pinner, Leiner, and Zavod were among the many who emphasized this point. However, these same writers pointed out that fibrothorax and the "imprisoned" lungs appeared to be exceptions to this rule. In these extrapulmonary complications they showed that the roentgenogram was fairly representative of true functional division as determined by bronchospirometry. Our observations were in agreement with their impression.

Effect of duration of collapse on return of function. It has been suggested that lungs collapsed for long periods of time may undergo parenchymal changes which might interfere with recovery of function upon re-expansion. In our patients there was no evidence of any relationship between duration of collapse and the degree of functional recovery (Fig. 10). In general, the patients whose disease was of shorter duration showed a greater return of function but only because they often had less parenchymal disease than the patients with longstanding collapse. The lung of C.C. which was the site of a minimal tuberculous infection had been collapsed for 72 months but nevertheless showed excellent return of function (Table II). L.L. with moderately advanced disease, whose lung had been collapsed for only 7 months, showed little improvement (Table III).

Bacteriology of the pleural fluid. The immediate indication for decortication in most of the cases was infection of the pleural fluid. While this complication was a most important factor in the patient's immediate clinical state, it had little bearing on the functional outcome. In Figure 11 the cases were arranged according to the presence or absence of demonstrable tuberculous infection of the pleural fluid. Cases R.W. and R.M., classified here as "Mycobacterium tuberculosis absent" had Clostridium welchii and Staphylococcus aureus empyemas. Increase of function was slightly less in the group with tuberculous empyema but the presence of such infection by no means precluded satisfactory re-expansion and a substantial increase in function.

Purulence of the pleural fluid. The type of pleural fluid was another basis for classification in Figure 11. The terms "clear" and "cloudy" were based on gross observation of the fluid obtained by preoperative thoracentesis. "Purulent" fluid, observed during operation or on thoracentesis, was thick, creamy pus or a sediment amounting to more than one-half of the volume of the specimen. The type of fluid may have been of considerable importance in judging the gravity of the clinical picture but it had little to do with restoration of function. Indeed, some of the best results were observed in cases in which frank pus was present.

Relationship of postoperative time interval to return of function. The return of function following decortication was usually gradual and

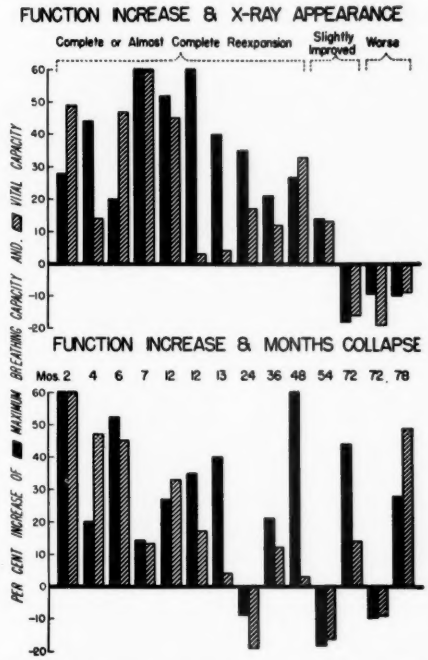
FUNCTION INCREASE & X-RAY APPEARANCE
Complete or Almost Complete Reexpansion
Slightly Improved
Worse
PER CENT INCREASE OF ■ MAXIMUM BREATHING CAPACITY AND ▨ VITAL CAPACITY
FUNCTION INCREASE & MONTHS COLLAPSE
Mos. 2 4 6 7 12 12 13 24 36 48 54 72 72 78
PER CENT INCREASE OF ■ MAXIMUM BREATHING CAPACITY AND ▨ VITAL CAPACITY

Fig. 10. Maximum breathing capacity and vital capacity expressed as per cent change due to decortication related to amount of re-expansion as judged from the chest film (top) and related to the length of time that the lung had been collapsed prior to operation (bottom).

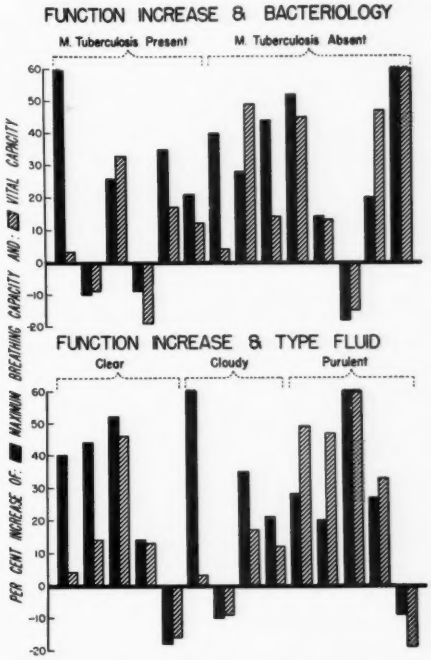
FUNCTION INCREASE & BACTERIOLOGY
M. Tuberculosis Present
M. Tuberculosis Absent
PER CENT INCREASE OF ■ MAXIMUM BREATHING CAPACITY AND ▨ VITAL CAPACITY
FUNCTION INCREASE & TYPE FLUID
Clear
Cloudy
Purulent
PER CENT INCREASE OF ■ MAXIMUM BREATHING CAPACITY AND ▨ VITAL CAPACITY

Fig. 11. Maximum breathing capacity and vital capacity expressed as per cent change due to decortication related to the presence or absence of tuberculous infection of the pleural fluid (top) and related to the appearance of the empyema fluid (bottom).

often continued for a period of months or even years (Fig. 12). This fact was not clearly demonstrated in previous reports because patients were seldom studied more than once after operation and usually the observations were made in the immediate postoperative period when performance of tests requiring maximal voluntary effort was impeded by pain. Actual diminution of voluntary efforts were observed for several weeks in patients who later showed a satisfactory improvement. Most of the patients studied showed progressive improvement during the entire period of observation which, in some cases, was 2 or 3 years. When extensive parenchymal disease was present the immediate postoperative loss was more marked and the gradual improvement less.

Bronchospirometric study demonstrated that, as the total function increased, a greater proportion of that increase was contributed by the lung operated upon (Table II). That this increasing contribution was gradual is strikingly illustrated by patient M.W. (Fig. 8) in whom bronchospirometry showed a functionless lung 3 months after decortication. At this time a dense homogeneous shadow was seen over the affected lung in the roentgenogram. Three years later the shadow had disappeared and re-expansion of the underlying lung had taken place. Repeated bronchospirometry showed increased function of the affected lung accompanying the roentgenographic changes. Studies of R.W. with traumatic hemothorax revealed striking improvement of ventilation 2 weeks after operation with continuing impairment of oxygen consumption of the affected lung. Five and one-half months later resumption of nearly normal participation was apparent (Fig. 2).

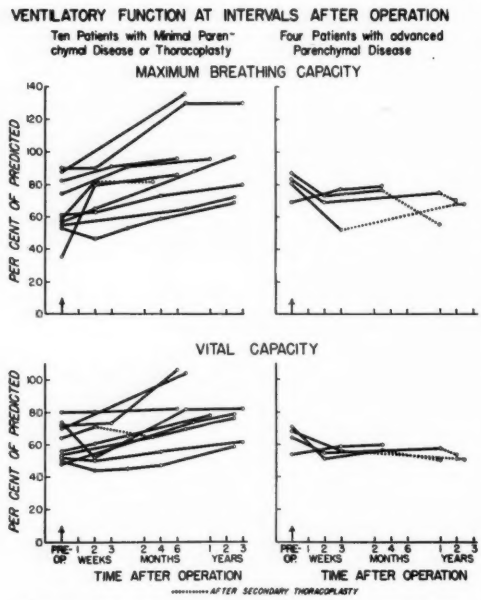

Fig. 12. The effect of the passage of time on the return of pulmonary function after decortication.

The effect of pleural disease on pulmonary function. Many authors have noted that pleural disease causes a loss of pulmonary function which is out of proportion to the amount of involvement shown by the roentgenogram. Parenchymal disease, on the other hand, causes relatively little loss in its early stages, and may bring about only moderate pulmonary disability even when quite far advanced. The first 8 patients (group I) had either no parenchymal involvement or lesions of an extent which are not commonly associated with functional impairment. It seems reasonable to assume that the functional losses found in these cases, both before and after operation, were due entirely to pleural disease. There was evidence in only 1 instance (F.G.) that longstanding collapse on one side had caused overdistention and emphysema of the opposite lung. The respiratory defect in the patients with more advanced parenchymal involvement (group II) was thought to have been caused chiefly by the pleural disease.

Constrictive pleuritis, present in all of our patients, caused a decrease of lung volume. The amount of compression was shown to have a direct bearing on the preoperative loss of function. Re-expansion probably accounted for the earlier postoperative gains.

Any chronic pleuritis with or without constriction imposes a mechanical disadvantage on the lung by causing a loss of parietal elasticity. This is chiefly due to pleural symphysis and the deposition of interpleural fibrous tissue. The loss of elasticity persists in some degree after even the most satisfactory decortication and probably accounts for the fact that pulmonary function seldom returns to the predicted normal postoperatively. Other irreversible changes, such as overdistention of the good lung, shift of the mediastinum, elevation of the diaphragm, and decrease in size of hemithorax may also contribute in some cases to incomplete restoration of function.

Roentgenographic shadows caused by interpleural fibrous tissue tend to become less dense with the passage of time, suggesting that some resorption of the encapsulating cortex may occur and that the parietal envelope may become less rigid. This process was apparently largely responsible for the gradual increase in function seen when patients were studied at increasing intervals after operation. There may also have been some slow improvement in the tone of the respiratory musculature.

The residual defect tends to follow a set pattern. For instance, 11 of our 14 patients showed a greater reduction of vital capacity than of maximum breathing capacity (Figs. 1, 7, 8). This would seem to indicate that it is the extremes of the ventilatory excursion that are impeded by the rigid pleural envelope. Between these extremes lies an area of respiratory mobility which may be exploited with relative efficiency. This observation is borne out by the bronchospirograms. In almost every case the affected lung utilized a greater proportion of its maximum possible (vital capacity) excursion in the performance of quiet respiration.

Jacobaeus, in some of the earliest reported bronchospirometric studies, observed the marked deleterious effect which pulmonary disease exerts on oxygen uptake. He found that oxygen uptake was sharply decreased and that ventilation was affected to a lesser

extent in every case of unilateral pulmonary disease. His findings were confirmed and amplified by Pinner, Leiner, and Zavod who noted that the defect of oxygen uptake was particularly severe in the presence of pleural complications. Among 90 cases of pulmonary disease they found 11 instances in which one lung was damaged so severely that it was responsible for less than 25 per cent of the total oxygen uptake. In every one of these there was evidence of some pleural involvement. Ventilation was much less affected.

A disproportion between ventilation and oxygen uptake can be best appreciated by comparing the ventilatory equivalents calculated for the two lungs separately. The values obtained during bronchospirometry are usually higher than those calculated from a resting spirogram because of the voluntary hyperventilation brought about by the manipulations necessary for the performance of bronchospirometry. In spite of this the uninvolved lung frequently had a ventilatory equivalent below 2.5 suggesting that it was placed under stress, probably because it did the major share of the respiratory work through a single lumen of the narrow catheter. The affected side invariably showed an elevated ventilatory equivalent. In order to eliminate the effect of voluntary hyperventilation the ventilatory equivalents of the involved lung are presented as per cent of the ventilatory equivalent on the well side in Figure 13. In 89 patients with moderately or far advanced parenchymal disease the two equivalents bore a relatively close relation to each other. The mean equivalent on the affected side was only 43 per cent larger than that of the good lung. The greater effect of pleural disease on oxygen consumption than on ventilation was shown by the ventilatory equivalents of 42 patients with adhesive pleuritis. The equivalent on the affected side was 155 per cent larger than on the good side. In other words, the diseased lung had to breathe three times as much air for the same oxygen uptake than the well lung. The disproportion between respiration and ventilation was even greater in the patients of the present series, all of whom had constrictive pleural disease (Fig. 13). The postoperative data still showed a greater disproportion between oxygen uptake and ventilation than patients with parenchymal disease. The defect pertaining to pleural involvement had been diminished but not cured by decortication.

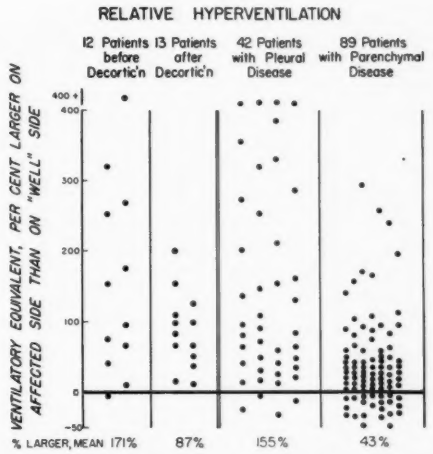

Fig. 13. The ventilatory equivalent of the involved lung expressed as per cent of the ventilatory equivalent of the uninvolved lung in our patients before and after decortication and in other patients with pleural disease and with parenchymal disease.

In the absence of arterial hypoxia the differential oxygen uptake is indicative of the relative share of the right cardiac output reaching each lung. When oxygen absorption of one lung is greatly reduced without a proportionate decrease in ventilation it means that the blood flow is meeting with increasing resistance on that side although the airways are still relatively patent. Pleural disease, by constricting and reducing the volume of the lung, apparently increases peripheral resistance of the pulmonary capillary bed and thereby reduced blood flow. The reduction of pulmonary volume does not seem to have an equally deleterious effect on ventilation. Ventilation without diffusion appears to be the rule in partially collapsed lungs while perfusion and ventilation appear to be decreased to a much more nearly equal degree by parenchymal disease. In certain types of parenchymal disease, particularly the fibroses, pneumonoconioses and pneumonias perfusion seems to persist for sometime even after ventilation has been greatly impaired. This prob-

ably accounts for the fact that arterial hypoxia is almost never seen during pneumothorax therapy, even though collapse may be extensive and bilateral, while it is common in the parenchymal disease mentioned.

SUMMARY

The pulmonary function of 14 patients with unilateral constrictive pleural disease and hydropneumothorax was studied before and at intervals up to 3 years after surgical decortication of the lung.

Overall function was evaluated by maximum breathing capacity, vital capacity, and exercise ventilation. Participation of affected side was determined by bronchospirometry.

Preoperative studies showed a severe, restrictive ventilatory insufficiency which bore a relationship to the amount of collapse seen on the roentgenogram. This was due to a lack of respiratory activity on the affected side with severe reduction of oxygen uptake and vital capacity. Resting ventilation of the diseased lung was only moderately impaired.

Restoration of function after decortication was most closely related to the presence or absence of pre-existing parenchymal disease.

Early postoperative studies showed moderate improvement of function in patients with no or minimal parenchymal disease and a decrease in function in patients with moderate or advanced disease.

Serial studies, performed up to 3 years after operation, showed a progressive gain in function during the entire period of observation. Patients with little parenchymal disease ultimately showed a mean increase of 47 per cent in maximum breathing capacity and a 31 per cent increase of vital capacity. Patients with advanced parenchymal disease did not overcome the sharp reduction of function noted during the early postoperative period. Their mean maximum breathing capacity was 6 per cent less and the mean vital capacity 16 per cent less than before operation. In patients with little parenchymal involvement bronchospirometry showed a mean increase of 172 per cent in oxygen uptake, 136 per cent in vital capacity and 53 per cent in resting ventilation by the involved lung. In patients with advanced parenchymal disease the relative participation by the diseased lung was not altered by decortication.

The ultimate gain of function was not influenced by the preoperative duration of pulmonary collapse, by the presence or absence of infection in the pleural fluid, or by the purulence of the fluid. The gain of function bore a close relationship to the amount of re-expansion seen in the chest films. Patients in whom only visceral decortication was done showed improvement comparable to that seen in patients with complete visceral and parietal decortication.

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SECRETORY DISEASE AND PLASMA CELL MASTITIS IN THE FEMALE BREAST

Roentgenologic and Pathologic Studies

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SECRETORY disease and plasma cell mastitis have been recognized in the female breast for many years. Nevertheless it is remarkable how seldom the diagnosis is made, even by pathologists. The object of this communication is to achieve wider recognition of these entities and to dispel some of the fallacies which have arisen regarding them. Roentgenologic studies have proved especially valuable in the elucidation of this subject and in demonstrating that secretory disease and plasma cell mastitis are one nosologic entity.

Secretory cystic disease has been described under the rather confusing title of "comedomastitis." The condition represents an abortive attempt at secretion on the part of a nonpuerperal breast and is not an inflammation; the term "secretory" is therefore appropriate. Although inflammation may be a sequel it is not present at the onset. The qualification "cystic" should probably be dropped, because although cysts occur, the ducts are often uniformly dilated rather than strictly cystic. In our classification of diseases of the breast (2, 3) we have substituted "mazoplasia group II" for the old terms "simple cystic disease" because we realized that the important factor was not the cysts, but uniform hyperplasia of all the components of the duct wall; the cysts are secondary. The underlying pathology of secretory disease is proliferation followed by differentiation into secretory cells which finally degenerate and are cast off into the lumen of the duct. Often the myoid is also hyperplastic and since the myoid is the source of the intraductal fibrous tissue, there can be growth of the duct wall along with secretion into the duct lumen. Considerable dilatation of the duct lumen is thus rendered possible, but the dilatation is never as great as in advanced cases of mazoplasia II and cysts are not formed to the same extent. Secretory disease, however, may be engrafted on mazoplasia II or on other dysplasias.

Plasma cell mastitis is a complication of a secretory disease. Textbooks state that it is rare. Actually, the focal form is common, but often passes unrecognized by pathologists and surgeons who think only of the generalized form. Haagensen opportunely has called attention to the focal form already discussed in 1939 by Rodman and Ingleby. Plasma cell mastitis is said to be seldom bilateral, but in our series, every case of secretory disease with or without plasma cell mastitis that came to operation was shown by roentgenology to be bilateral. This is an important diagnostic point in the differentiation of plasma cell mastitis from abscess in the nonpuerperal breast. Roentgenologically, abscess resembles plasma cell mastitis, but is unilateral. Roentgenological studies have convinced us that, fortunately for the women concerned, most cases of secretory disease are asymptomatic. Until routine x-ray examinations are made it will not be possible to determine how often it is present in otherwise normal women, but it has been observed as an incidental finding at autopsy in the postmenopausal age group. We have found it bilaterally in the breasts of women roentgenographed for other lesions, and have made the diagnosis in some who were not operated upon. Here, with 1 exception, we discuss only primary cases, roentgenographed for definite symptoms, and verified by operation.

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Fig. 1. Case 1. Right breast. Secretory disease with plasma cell mastitis.

Fig. 2. Case 1. Left breast. Minimal secretory disease is shown.

CLINICAL STUDY

Of 300 cases of breast disease examined to date, there were 24 cases of secretory disease. Three of these were cases of lactation in nonpregnant young women. We regard this as the early, reversible stage of the lesion. Two were operated upon, 1 for a concommitant fibroadenoma. Through the courtesy of Dr. Paul H. Fried we were able to follow the third case for many weeks. There was milk-like discharge from both nipples; the secretion was more abundant after the onset of menstruation, at which time colostrum cells were present. Dilated ducts were present in both breasts. These reached their greatest diameter before the menstrual period. After treatment with testosterone the discharge ceased and there was only slight suggestion of the former masses. Of course, no operation was performed. The x-ray films taken at intervals were of considerable interest. At first, the breasts presented an appearance mimicking that of normal lactation with occasional cysts. After receiving testosterone, the homogeneous opacity due to glandular development resembling lactation had largely disappeared.

The average age of the remaining patients was 47 years; the oldest was 67, the youngest 34. The duration of symptoms was usually short, under 1 month in 18 patients. This is in sharp contrast with the cases of mazoplasia in which the duration of symptoms is more often a matter of years. In contrast also are the marital histories which are nearly always normal. Our patients were all married, and although secretory disease may be found in single women, it is our impression that this occurs rarely. All but 1 nursed their children, but 5 had puerperal mastitis. One stopped nursing because of influenza and 1 because of appendicitis. In 2, trauma was a direct antecedent. Sixteen cases were complicated by

Fig. 3. Case 2. Left breast. Secretory disease with plasma cell mastitis.

plasma cell mastitis. The others showed minimal inflammation, not diagnosable histologically. The rare generalized form of plasma cell mastitis, the only one which has received adequate recognition to date, unfortunately did not occur in the present series. The dividing line between secretory disease and plasma cell mastitis is difficult to draw. Symptoms of both conditions are similar, but generally milder in secretory disease. Widespread changes in the x-ray film point to plasma cell mastitis.

Secretory disease is most commonly found in the nipple area, occurring at this site in 16 of our 24 cases. It may be asymptomatic even when complicated by a mild degree of plasma cell mastitis. When symptoms are present the most characteristic manifestations are a painful swelling and discharge from the nipple. A mass, varying in size from a few millimeters to 3 or 4 centimeters in diameter, was present in 19 cases. The mass was often soft or indefinite in outline, but sometimes hard. In 1 case a dilated duct was palpable, in 2 no

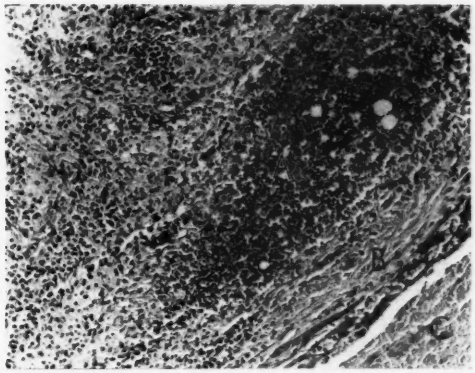


Fig. 4. Paraffin section from Case 2, showing secretory disease and plasma cell mastitis: *A*, necrotic duct; *B*, degenerating colostrum cells in epithelium of adjacent larger duct; *C*, degenerated secretion in large duct not as yet involved in the inflammatory process.

swelling could be felt. Discharge from the nipple, either intermittent or continuous was a presenting symptom in 8 cases. It was usually thick, sometimes inspissated; in 3 it contained blood. There was no correlation between the presence or absence of pain and nipple discharge.

Secretory disease, once established, remains indefinitely. There are usually no symptoms, but exacerbations may occur. For example, 1 patient who had complained of pain and swelling for 3 weeks had been operated on 6 years before for an exactly similar secretory lesion.

ROENTGENOLOGY

The roentgenologic findings in secretory disease in the older age group to which most of the cases belong are pathognomic. The lesion is most easily identified when it is situated in the nipple area (Figs. 1, 2, 3, 5). The ducts leading from the nipple are visible because they are distended. Many or all may be involved; it is rare to find only one duct affected. Their course toward the base of the gland is tortuous. They end in club-shaped dilatations, or sometimes in flame-like projections. Occasionally a group of ducts may form a coalesced mass, sometimes cyst-like in appearance, localized to a small area just under the nipple. Rarely, an isolated duct may be dilated and since the dilatation is not always uniform, a beaded appearance results,

Fig. 5. Case 3. Left breast. Secretory disease with plasma cell mastitis.

simulating the picture usually associated with papilloma.

Since the presence or absence of plasma cell mastitis is sometimes hard to determine, even microscopically, and when present may be limited to a few microscopic fields, it is obvious that it will not always be visible in the x-ray film. A sizable focus is seen in the x-ray film as a homogeneous, coarsely tentacled density, easily visible in older breasts where there is much perifocal fat. The margins of these masses extend in flame-like projections along the line of the trabeculae. In the younger group of patients, the most striking x-ray finding is the uniform ground glass appearance of the affected area. The trabecular markings are either absent or blurred as if smudged by an eraser. This appearance is also characteristic of lactation. The blurred patches may be focal or widespread. Microscopically the

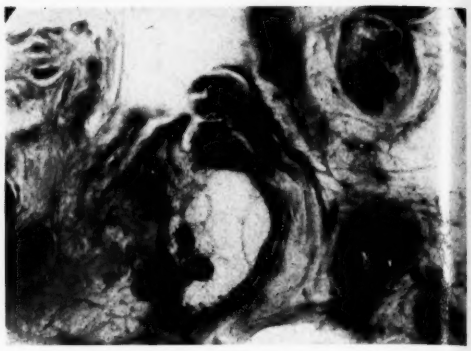
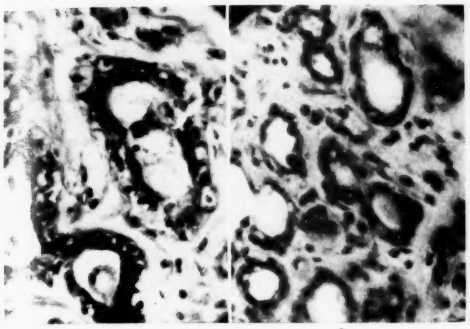


Fig. 6. Case 3. Slicer section. Long-standing secretory disease; in one duct the secretion has dropped out in processing.

lobules in those areas often resemble those of pregnancy or lactaction. If cysts are present, as they often are, the anterior margin of the breast has an undulating contour due to the bulging of these cysts. Under these circumstances, the appearance of the breast resembles that of mazoplasia II, but close inspection reveals the curious blurring or loss of trabecular architecture mentioned (Fig. 8).

Difficulty in diagnosis arises when mazoplasia II and secretory disease are present in the same breast. Large cysts can be visualized by use of up-to-date x-ray technique and in any case, they are easy to separate from the much smaller secretory cysts. Sometimes, small mazoplastic and secretory cysts are intermingled in one quadrant. In a case of this type the diagnosis could only be made if a fairly large area of plasma cell mastitis was also present, when the characteristic fuzzy tumor should be seen. Secretory cysts may be intermingled with other lesions of Schimmelbusch disease or mastopathy. Obviously they would be indistinguishable roentgenologically, nor would there be any object in making the diagnosis; they are only an insignificant part of the general dysplasia.

Several cases of mixed mazoplasia or mastopathy and secretory disease could be determined roentgenologically and the histories indicated the sequence of events. For example, one patient with a history of 6 weeks' nipple discharge, had been receiving injections of estrin monthly for 3 years, a



a b

Fig. 7. Case 4. a, Acini with secreting cells. b, Breast 4 days postpartum, early lactation involution.

procedure which can be guaranteed to produce mazoplasia with cysts in the majority of women. Her x-ray film is characteristic of mazoplasia group II with superimposed secretory disease and plasma cell mastitis. Another patient had 7 years' history of premenstrual breast pain, swelling, and uterine myomas, a story characteristic of mazoplasia, but not of secretory disease.

Fig. 8. Case 4. Right breast. Secretory disease with acute plasma cell mastitis following trauma.

PATHOLOGY

If nipple discharge is present, the diagnosis can nearly always be made by examination of the smear (Fig. 10). Unless degeneration of duct contents is far advanced, colostrum cells are easily recognizable. The fact that fat laden histiocytes as well as secretory cells from the epithelium contribute to the "colostrum" and, at this stage, are indistinguishable from each other, has led to a certain confusion. The participation of histiocytes in the secretion should not cause surprise; the histiocyte is a normal component of early pregnancy. Besides colostrum, inflammatory cells of various kinds are apt to be present and would be expected where plasma cell mastitis is a complication. In plasma cell mastitis fatty acid crystals may be found and even giant cells and "rosettes" although these last are not common in the smear. Red blood cells in various stages of degeneration are seen if there is ulceration of the duct.

The gross appearance of secretory disease (Fig. 11) with worm-like casts exuding from the dilated ducts is too well known to need description here. In uncomplicated cases the inspissated material is white or yellowish. When it shows red, green, or brown discoloration, there is likely to be plasma cell mastitis. The mastitis, if sufficiently extensive, presents a yellow necrotic area, often with discolored patches. Microscopically, the secretion in the ducts may be amorphous with occasional shadows of colostrum cells, or it may be packed with colostrum and inflammatory cells, together with fatty acid crystals (Fig. 12). The state of the lining epithelium varies. The early phase is one of hyperplasia with differentiation of many of the cells to the secretory type. It is not uncommon to find ducts lined by heaped-up cells with clear vacuolated cytoplasm having their origin in the epithelium or in fat-laden histiocytes which have migrated there. The hyperplasia is sometimes sufficient to produce small polyps, but these generally disintegrate. The late stage is marked by degeneration of the secreting epithelium.

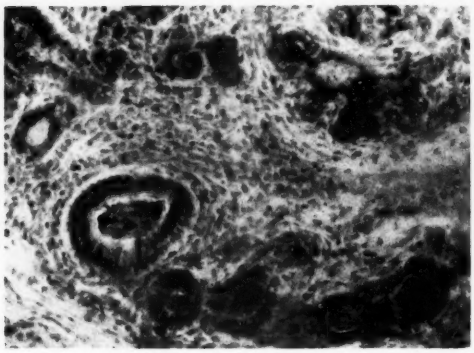


Fig. 9. Frozen section from Case 4; stained with hematoxylin and scharlach R, showing part of a lobule and a small duct. The lumens of some of the acini are filled with fatty secretion as is that of the duct. The surrounding tissue is heavily infiltrated with inflammatory cells.

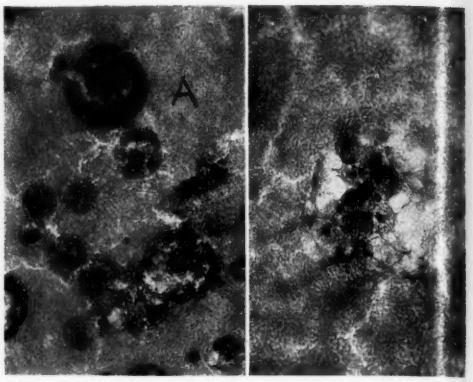


Fig. 10. Secretory disease, discharge from both nipples a, left, Smear from right nipple: swollen colostrum cells containing numerous lipoid granules. b, Smear from left nipple: amorphous fatty material in which shadows of degenerated colostrum cells can be occasionally recognized.

When this happens on a large scale the duct is lined by a flattened membrane. Secretion also may be found in ducts lined only by the usual columnar cells. This would indicate that the secretion originates farther back in the mammary tree. Examination of the adjacent lobules often reveals ductules filled with secretion and lined by cells resembling those seen in lactation, although not as a rule so abundant. This is probably why the x-ray film is apt to mimic that of the lactating breast. It should be noted that the lobular secretion is frequently not accompanied by inflammation, which is evidence that the mastitis is a secondary phenomenon.

The variability of the histologic picture in generalized plasma cell mastitis is well known and the focal type is no exception, but since the areas involved are so much smaller, not all the variations can be expected to be present in any one case. The principal lesions to be looked for are: (a) Ulceration of the wall of a duct containing secretion may be present. These ulcers are the source of blood in the nipple discharge. (b) There may be necrosis of a duct with destruction of its wall so that the original structure may be hard to recognize. The necrosed area is surrounded by a broad zone of inflammatory cells. The inflammatory exudate may break through the wall of an adjacent duct with invasion of its lumen by inflamed granulation tissue. This inflamed tissue may then appear as a polyp-like mass within the duct. (c) The inflammatory cells may be of any or every type. Fat containing histiocytes are sometimes numerous. Giant cells and fatty acid crystals are often, but not always present. Rosettes are comparatively rare. (d) Fibrosis is a prominent feature if the mastitis has been present for some time.

DISCUSSION

Secretory disease, while allied to other forms of mammary dysplasia, deserves to be classified as a distinct entity. It is a much milder disorder than its rather bizarre appearance would suggest, and it is only important as the precursor of plasma cell mastitis. Since the essential feature is differentiation of epithelial cells, followed by degeneration and shedding, carcinoma does not arise in the affected ducts.

The view that plasma cell mastitis is a complication of secretory disease is based on the following evidence. In the first place, secretory disease is invariably present along with the mastitis and is recognizable even in advanced, generalized cases. The reverse is not true. Secretory disease often occurs alone, and even in extensive mastitis thorough examination will reveal ducts and lobules which are not inflamed but contain secretion. Since

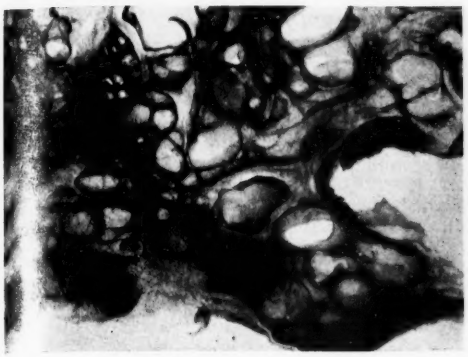


Fig. 11. Secretory disease: gross appearance of dilated ducts.

Fig. 12. Focus of plasma cell mastitis: paraffin section showing giant cells and clefts filled with fatty acid crystals.

the type of exudate is similar to that seen in fat necrosis in other situations, it seems probable that inflammation is caused by the breakdown of fat derived from the degenerated colostrum cells. Evidence that fat necrosis does occur is found in the fatty acid crystals so commonly seen in the sections. Protein breakdown may also play a part. Many years ago Ingleby was able to reproduce the picture of plasma cell mastitis in the breasts of rabbits by injections of pancreatized cream and milk in the breasts.

Clinical considerations such as the sudden onset of a painful mass, sometimes showing discoloration through the skin, suggest that symptoms are due to inflammation and not to the mere presence of secretion in the ducts. A blow on the breast of insufficient force to cause injury in a normal woman, initiated the symptoms in 2 cases. Rupture of the wall of an affected duct might well be sufficient to start the inflammatory reaction. The remote effect of puerperal mastitis is not so clear. Our case histories show that it was important, but at present the connecting links are missing.

Plasma cell mastitis tends to subside gradually, and treatment is not necessary except as the patient's comfort demands it. Cutler believes that irradiation hastens involution of the lesion. It could not be expected to alter the condition of inspissated secretion in the ducts where secretory disease alone is present. If surgery is undertaken, it is important to remove the entire diseased area. In 1 case in which this was not done, a discharging sinus resulted, necessitating a second operation. The material from the sinus did not contain bacteria and the smear was typical of plasma cell mastitis.

ILLUSTRATIVE CASE REPORTS

CASE 1 (Figs. 1 and 2). Secretory disease and plasma cell mastitis. This patient, 46 years old, had a soft, painful mass, 1.5 centimeters in diameter, just beneath right nipple, for 1 week. The nipple was inflamed and a thick discharge could be squeezed from it.

The x-ray films show bilaterally retracted nipples with thickened areolae. The lead shot on the skin marks the spot of localized pain and tenderness in the right breast. The dilated ducts beneath the nipple are seen as a single mass, resembling the stem of a torch which has flame-like extensions fading out toward the base of the breast. At the junction of the stem and flames of the torch is an indefinite mass of homogeneous density resembling a patch of lactating tissue, characteristic of plasma cell mastitis. This is distinct from carcinoma because the fine spicules of malignant infiltration are lacking. Another diagnostic point hinges on the difference between the smaller size of the palpable tumor and its size in the x-ray film. Malignant masses are smaller in the x-ray film than their palpable size.

The left breast (Fig. 2) reveals a lesion similar to that in the right breast, but the lesion is less advanced and lacks the tumor-like infiltrations of plasma cell mastitis.

Pathologically, the ducts grossly contained worm-like casts. One duct beneath the nipple was filled with pus-like material. Microscopically, secretory disease with plasma cell mastitis was evident.

CASE 2. Secretory disease and plasma cell mastitis. This patient, 67 years old, had a firm painless

mass above the left nipple, noted for 3 days. At operation it was noted that dilated ducts filled the thick greenish material.

X-ray film (Fig. 3) shows that beneath the left nipple is an irregular mass with short flame-like extensions. These follow the direction of the trabeculae and gradually fade out. (Extensions from a carcinoma are sharp and cut across the trabeculae.) The skin of the areola is thickened, but the nipple is not displaced. The opposite breast showed a similar lesion, but not as advanced.

Pathologic sections show groups of dilated ducts filled with necrotic material in which are shadows of colostrum cells. In one place there are necrotic areas in which remains of ducts can still be distinguished. These are surrounded by masses of inflammatory cells, which can be seen penetrating the wall of adjacent ducts hitherto not involved in the inflammatory process (Fig. 4).

CASE 3 (Figs. 5 and 6). Plasma cell mastitis following trauma, in a breast the seat of long standing secretory disease. This patient, 50 years old, bumped her left breast 2 weeks before examination. Within 4 hours she felt pain. On examination, there was redness of the skin and an indefinite palpable mass 3 centimeters in diameter, above the level of, and beneath the nipple area.

X-ray film (Fig. 5) shows nipple retraction. Both breasts present an opacity beneath the nipple, but in this left breast the localized subareolar opacity extends with torch-like and flame-like projections. This is the area of plasma cell mastitis.

Pathologically (Fig. 6) the ducts in the nipple area are filled with inspissated secretion and surrounded by dense fibrous tissue. Paraffin sections showed plasma cell mastitis.

The findings in this case indicate that the patient had asymptomatic secretory disease, probably for years, and that trauma initiated a sudden flare-up of plasma cell mastitis.

CASE 4. Secretory disease in a woman of childbearing age. Plasma cell mastitis following trauma to breast. This patient, 35 years old, bumped her right breast against a door 6 days before examination. The injury was slight. She first noted a painless mass soon after injury, but 2 days later the mass became painful and the skin over it was reddened. There was a slight discharge from the nipple. On examination, a tender mass 4 centimeters in diameter was found in the nipple area.

In the x-ray film (Fig. 8) the parenchyma has a uniform ground-glass appearance. The anterior bulge in the mammary tissue below the nipple, as well as thickening of the overlying skin, is caused by inflammatory swelling. Marker on skin localizes the area of greatest tenderness.

Pathologic specimen shows a severely inflamed area with brownish, worm-like casts exuding from dilated ducts. Paraffin section reveals severe plasma cell mastitis in most of the areas examined. But in the uninflamed parts, the ducts contain secretion and the cells lining the acini are mostly of the secretory type, as in pregnancy (Fig. 7). In a nearby lobule, the secreting cells are in the process of degeneration and fatty debris fills the ductules. Frozen sections stained with scharlach R showed fatty material in ducts and acini (Fig. 9).

SUMMARY

Study of 24 cases of secretory disease revealed that the condition is usually bilateral and that it is more common than is generally thought.

In the majority of cases, due to chemical irritation, inflammation of the type known as plasma cell mastitis supervenes. In general, it is the plasma cell mastitis rather than the secretory disease which is responsible for the symptoms, although nipple discharge is common to both.

The diagnosis may be suspected from the history and physical examination, and is confirmed in most cases by the characteristic x-ray findings and by examination of a smear from the nipple discharge.

Secretory disease and plasma cell mastitis are not precancerous conditions. Treatment is optional, but if surgery is undertaken the whole of the diseased area should be excised, otherwise complications such as discharging sinuses may follow.

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THROMBOSIS OF THE TERMINAL AORTA

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OCCLUSIVE thrombosis of the terminal aorta is a pathologic and clinical disease entity that usually can be benefited by surgery. Leriche (1c), of France, was the first to describe the clinical syndrome in 1940. Earlier publications established its occurrence through study of necropsy specimens: Graham in 1814 recorded his observations on one museum specimen and Welch (19) of Johns Hopkins Hospital in 1899 reported 7 cases of primary thrombosis of the abdominal aorta. It is possible now to correlate long term clinical observations and results of treatment with necropsy pathologic findings. The purpose of this report is to present this material so that occlusive thrombosis of the terminal aorta will be recognized more readily and the condition be properly treated.

MATERIAL

From 1934 to 1951, 29 patients with complete occlusion of the abdominal aorta were observed and studied; this series represents 1.6 per cent of the patients examined for peripheral circulatory disease of the lower extremities. Twenty-one (72 per cent) were observed for more than 1 year, and 9 (31 per cent) for more than 5 years. Twelve patients are being followed currently, having been seen over a period of from 2 to 9 years, and 6 patients who died after having been observed clinically from 2 to 7 years were necropsied. Complete peripheral vascular examinations were made on all patients and repeated follow-up examinations were made in 92 per cent of them.

CLINICAL SYNDROME

Etiologic factors. Twenty-five patients (86 per cent) were under 60 years of age or dated the initial symptoms before then; 17 (58 per cent) were between 50 and 60 years of age at the time of their initial examination, and only 4 were over 60 years. The average age of both the diabetic and nondiabetic males was 55 years, of the diabetic females 56 years, and of the nondiabetic females 61 years. Two nondiabetic patients, 1 male and 1 female, were 19 years of age at the time of their initial symptoms. The sex distribution was 13 females and 16 males; there were 4 diabetic and 9 nondiabetic females and 3 diabetic and 13 nondiabetic males.

Hypercholesterolemia of over 300 milligrams per cent was present in 62 per cent of the patients and only 1 had a total cholesterol value under 250 milligrams per cent. In the patient with luetic aortitis it was 260 milligrams per cent. It is probable that these values might have been reduced from previously higher levels, for most patients had found that they were benefited by restricted fat diets (Table I).

Symptoms. The onset of symptoms was insidious in 90 per cent and acute in 10 per cent of the cases. The average duration of symptoms was almost 3 years, and many cases were undiagnosed for 5 to 8 years despite competent medical examinations. Three acute cases were diagnosed within 3 weeks because the severity of the symptoms required early consultation.

Intermittent claudication was a primary complaint of 27 patients (93 per cent), with 22 bilateral and 5 unilateral cases. Fatigability and pains in the hips and thigh muscles were prominent symptoms in 17 cases (58 per cent), 15 of which were bilateral and symmetrical and 2 unilateral on the right side. Coldness of the feet and legs was not constant or troublesome. Impotence was not a complaint; only 1 patient had total impotence prior to his death at 49 years of age, after suffering with symptoms of severe peripheral circulatory deficiency since the age of 19 years. Nocturnal rest pains in the extremities were severe whenever infection or gangrene was present.

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TABLE I.—ETIOLOGIC FACTORS

	Males	Females
Sex, No.	16 (55%)	13
Diabetics	3	4
Nondiabetics	13	9
Age, years		
Average	56	55
Minimum	19	19
Maximum	64	71
Lues, No. cases	0	1
Cholesterol		
Average, mgm. per cent	336	316
Over 300, per cent	75	50
Under 250, per cent	10	0

Necrosis and gangrene of the toes were present in 9 cases and 8 of these healed, following local surgery and conservative treatment; 1 diabetic patient with infected gangrene had a satisfactory recovery after bilateral lumbar sympathectomy and transmetatarsal amputation. Four patients with gangrene and resistant infection in the foot did not respond to conservative treatment and required unilateral major amputations.

Cardiac disease, hypertension, cerebral thrombosis, or anemia was present in more than 75 per cent of the cases. Since the primary disease is not confined to the abdominal aorta, these complications occur as a part of a generalized arterial disease process. The presence of cardiac disease frequently makes it impossible to rule out embolism of cardiac origin as the cause of the aortic obstruction or of the cerebral accidents, but necropsy findings confirmed the clinical diagnosis of thrombosis. Anemia was present in 30 per cent of the cases, clinical or electrocardiographic evidence of cardiac disease in 50 per cent, and hypertension, either systolic, diastolic, or both, in 55 per cent. These conditions affect the peripheral circulation and contribute seriously to impending gangrene.

TABLE II.—DIAGNOSTIC CRITERIA FOR THROMBOSIS TERMINAL AORTA

	Per cent
Onset of symptoms	
Insidious	90
Acute	10
Intermittent claudication	93
Pains in hips and thighs	60
Absent femoral pulse	
Bilateral	64
Unilateral	27
Oscillometric index under 1 unit	
Right thigh	90
Left thigh	82
Calcification of abdominal aorta	85

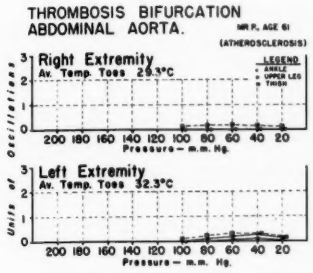
Infection is a serious complication in the presence of deficient peripheral circulation and gangrene. The poor circulation cannot supply sufficient concentration of antibiotic or chemotherapeutic agents to the involved area and the symbiosis of resistant organisms will further deprive the tissues of available oxygen. Rapid extension of the infection and gangrene may follow failure to control the infection.

Physical examination. Skin temperatures of the toes and feet may be within normal limits or vasodilator tests (reflex heat or drugs) usually produce good response. When normal temperature response does not occur, organic occlusion of the collateral channels or of the peripheral arteries can be expected. Most patients reacted favorably to the vasodilator tests, which is reliable prognostic evidence for the success of sympathetic neurectomy.

Peripheral arterial pulsations are usually absent, as are the pulsations in the iliac arteries, but in obese individuals palpation of the iliac arteries is not reliable. When the aorta is occluded incompletely by thrombosis, one or both iliac arteries and corresponding peripheral arteries may still pulsate. Also, with good collateral circulatory channels or canalization of the obstructing thrombus some peripheral pulsations may return.

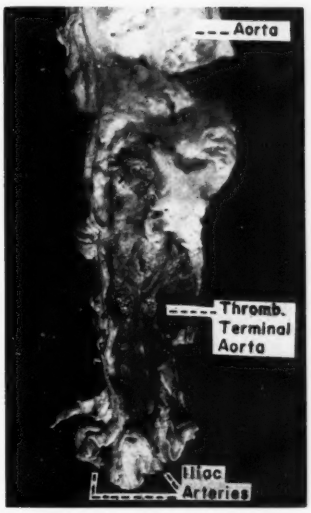
Oscillometric readings are frequently pathognomonic for occlusive thrombosis of the abdominal aorta. The readings at all levels of the extremity may approach zero but low oscillations are present usually due to collateral circulatory vessels or channels through unattached portions of the thrombus. The significant feature (Fig. 1a) is a shift of the curves to the right of the graphs (lower cuff pressures), instead of the maximum readings (index) being between the systemic systolic and diastolic pressures as occurs when the peripheral arteries are occluded. In the upper thigh the readings are usually under one unit of oscillation and at the knee zero.

The presence of "global atrophy of both lower limbs" is evidence of the chronicity of the circulatory deficiency. Leriche pointed out that the bilateral character of the atrophy may be overlooked. However, the peripheral



a

b



c

Fig. 1. a, Pathognomonic oscillometric curves (initial findings) made 15 months prior to death due to coronary occlusion. Complete bilateral obstruction of the main arteries in the lower extremities is evident. b, X-ray film showing calcification of terminal aorta. c, Necropsy specimen of thrombosed terminal aorta. No necrosis or gangrene of the extremity occurred during a period of 3 years despite extreme main artery obstruction.

arterial occlusion is not always symmetrical bilaterally. Whatever atrophy is present does not differ significantly from that resulting from gradual unilateral or bilateral peripheral circulatory deficiency (Fig. 3a).

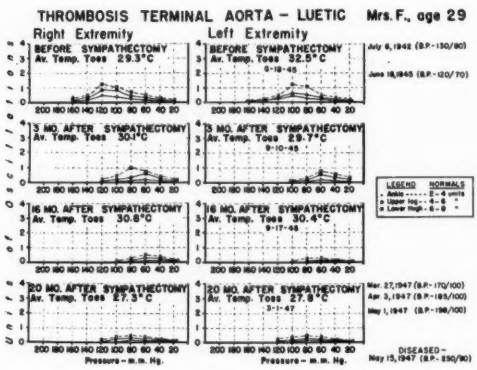
Laboratory findings. The urine should be examined for sugar, and the blood for hyperglycemia, hypercholesterolemia, and lues.

Roentgenography of the abdominal aorta, in particular the lateral view, is important in confirming the presence of arteriosclerosis (Fig. 1b). Although atherosclerosis and thrombosis are not revealed, the presence of calcification is evidence of more extensive atherosclerosis as well as arteriosclerosis. Only 3 nondiabetic patients failed to show some x-ray evidence of calcification of the aorta (Table II).

Aortograms will reveal the site, extent, and completeness of the aortic occlusion but they fail to show the important primary disease of the aorta that caused the thrombus. Leriche pointed out that the information obtained by aortograms should not be necessary to make the diagnosis.

PATHOLOGIC ASPECT

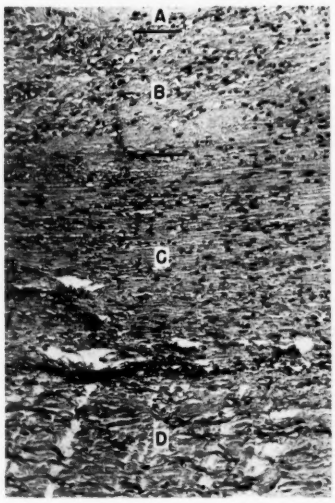
Disease of the abdominal aorta is the primary cause of the thrombosis. Atheromatous and calcium deposits in the wall of the vessel narrow the lumen gradually, and rupture of the intima with thrombus formation completes the occlusion (Fig. 1c). In the 6 necropsy specimens, large segments of the aorta and iliac arteries were involved in the disease process due to luetic aortitis in 1 case (Figs. 2a and 2b), and marked atherosclerosis and arteriosclerosis in the others. Fatal proximal propagating thrombosis occurred in 2 cases years after the initial thrombosis; 1 death resulted from the thrombus extending into the left renal artery, producing a Goldblatt kidney, and the other was due to obstruction of the inferior mesenteric artery, producing gangrene of the sigmoid. Surgical resection of the original thrombosed



a

Fig. 2. a, Oscillometric curves of patient with occlusive thrombosis of terminal aorta. Symptoms noticed first at 19 years of age and undiagnosed for 7 years. Clinical improvement, normal skin temperatures, and healing of amputation wounds for gangrenous toes after bilateral sympathectomy and pavaex treatments. She resumed her job as a standing factory worker until a propagating thrombus extended into and occluded first the left renal artery, producing a Goldblatt kidney, and then the right renal artery, causing uremia and death. b, Photomicrograph of transverse section of aorta just above bifurcation. The lumen is entirely occluded by fibroblastic granulation tissue (*C*) which has formed in the organization of a thrombus previously located at this level. The clear spaces in the fibroblastic tissue are new vascular channels. The intima, internal elastic membrane and media are normal except that the structure of the media (*B*) is interrupted in various places by penetration of blood vessels and by scarring. The adventitia (*A*) is very thick and dense and shows some of the characteristics of dense collagen formed in the course of repair of an inflammatory reaction. c, Photomicrograph of wall of aorta at upper limits of thrombus just below the renal arteries. The margin of an antemortem blood clot (*A*) is adherent to the greatly thickened intima (*B*). The thickening is due primarily to increase in fibrous tissue although the clear spaces indicate macrophages filled with lipids. This is an atheroma possibly the site of new thrombus formation. The media (*C*) is modified by inflammatory reaction and by disruption of the usual alignment of elastic network and smooth muscle cells. Considerable replacement by fibrous tissue. Adventitia (*D*) is thick and fibrous. Resection of original thrombosed segment of terminal aorta would not have prevented a new thrombus formation at this level.

b



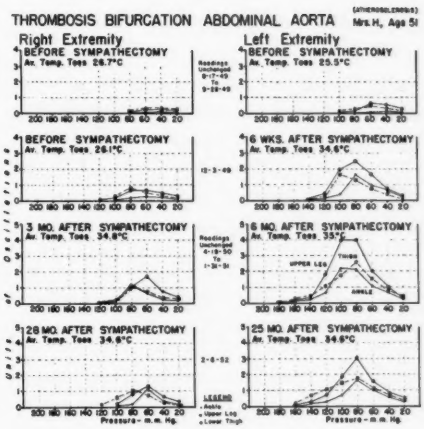
c

terminal aorta would not have prevented further thrombi formation on new sites of the extensively diseased aorta (Fig. 2c).

TREATMENT

Conservative or surgical treatment is directed to improve the collateral circulation to the lower extremities. This is most successful when the circulatory deficiency is caused by the aortic occlusion and there is minimum involvement of the peripheral arteries. Alternating positive and negative pressure treatments (pavaex) (7) produced excellent improvement and were used exclusively prior to 1946 on 12 of these patients. The objection to this form of treatment was the length of time required for furthering improvement. Bilateral lumbar sympathectomy is now being recommended routinely; 6 patients have had bilateral operations and 3 patients have had uni-

a



b

Fig. 3. a, Occlusive thrombosis of terminal aorta in 51 year old female. Note absence of "global atrophy" despite extreme main artery occlusion. b, Oscillometric curves for complete occlusion of the terminal aorta before and after lumbar sympathectomy. Condition had been undiagnosed for 8 years. Elevation of skin temperatures to normal levels, gradual elevation of oscillometric readings, and excellent clinical improvement followed surgery.

lateral operations. The advantages of the surgical procedure are that improvement in the peripheral circulation occurs more rapidly, and that sweating of the limbs ceases immediately. When the peripheral arteries are obstructed also, both sympathectomy and the pressure treatments are indicated. The combined treatment was used on 5 patients and major amputations were avoided.

Irrespective of the total blood cholesterol level, dietary restrictions of cholesterol-containing food is advisable. Most lipotrophic drugs have not proved successful in reducing the cholesterol. In some instances high cholesterol content of the blood (400 mgm. per cent and above) failed to respond to dietary restrictions or lipotrophic drugs over a period of years. During the period of postoperative convalescence, the cholesterol level in some cases dropped as much as 150 milligrams per cent and remained low for months before a slow rise occurred. Subjective improvement, with or without surgery, seemed to be related to the successful lowering of the blood cholesterol. With our present knowledge regarding atherosclerosis and arteriosclerosis an effort should be made to reduce the cholesterol content of the blood.

Anticoagulant therapy is not indicated because the usual insidious onset of the occlusion makes its use impractical. When acute occlusion occurs, as in 3 of our cases, the use of anticoagulants would not have changed the course of events; in the fatal cases 3 to 4 years elapsed between the initial thrombosis of the aorta and the propagating thrombus.

DISCUSSION

Both clinically and pathologically, thrombosis of the aorta may be difficult to differentiate from embolism, and most authors do not attempt to separate the cases of primary thrombosis from secondary thrombosis. This is apparent in reports based on necropsy records of Greenfield, Gross and Phillips, Siegel and Garvin, Lueth and Rothstein. However, Welch "without much confidence in accuracy" separated 59 necropsy cases into 45 due

to embolism, and 14 to thrombosis; of the 14 cases of thrombosis, only 7 were primary in the aorta. He noted that the condition was "not a senile affection" but occurred in individuals between the ages of 20 and 60 years with marked atheromatous changes in the aorta.

Resection of the thrombosed segment of the terminal aorta, as performed and recommended by Leriche, has been reported by a few American surgeons. Ortner's experience with 2 resections demonstrated that the proximal part of the thrombus could not be removed. Elkins' and Milanes' results with resection and sympathectomy were observed only a short time and the results were not impressive. Judging from the data given in various publications, the improvement following lumbar sympathectomy and resection of the terminal aorta was due probably to the sympathectomy alone in interrupting peripheral vasospasm of central origin.

Bilateral lumbar sympathectomy is the most advisable and satisfactory surgical procedure for occlusion of the abdominal aorta. Leriche(10), Gage, Holden, Holmans, Elkins and Reichert have reported good results following sympathectomy.

Impotence was mentioned by Leriche(11) and others as a prominent symptom that was relieved by sympathectomy. In our series, only 1 male, aged 49 years, had complete impotence for the last few years after suffering with occlusive thrombosis of the aorta for 30 years.

COMMENT

Occlusive thrombosis of the bifurcation of the aorta occurs more frequently than is recognized. The clinical diagnosis of primary thrombosis is made on the basis of long-standing bilateral peripheral circulatory deficiency, fatigability, and pains in the hip and thigh muscles, absent arterial pulsations, pathognomonic oscillometric readings, and calcification of the aorta. A massive thrombus may produce an acute onset, with rapid gangrene of an extremity only rarely. Aortograms are not necessary for diagnosis or for deciding the form of treatment to be used. Bilateral lumbar sympathectomy will improve the peripheral circulation, especially when the peripheral arteries are not involved seriously in the arteriosclerotic process. There is no medical treatment for the thrombus or arterial disease except to lower the cholesterol content of the blood. Excellent results have been observed clinically and demonstrated by objective tests (Figs. 3a and 3b) following adequate sympathectomy and reduction of the blood cholesterol.

Resection of the terminal aorta, as reported by Leriche, Elkins, Ortner and others, is not advisable even when the entire thrombosed area could be removed. The extent of the disease in the remaining artery makes closure of the lumen difficult, or impossible, and separation of the friable vessel from the perivascular adhesions hazardous. Collateral vessels and channels through the thrombus that maintain some peripheral circulation would be removed with the resection.

CONCLUSIONS

Occlusive thrombosis of the terminal aorta is a pathologic and clinical disease entity that should be recognized early in order to be benefited by surgery.

The clinical syndrome should be recognized without difficulty when the occlusion of the bifurcation is complete. Oscillometric readings are pathognomonic, and the skin temperature response to vasodilator tests will demonstrate the adequacy of collateral channels and patent peripheral circulatory vessels.

The primary disease of the aorta that leads to thrombosis is almost always atherosclerosis and arteriosclerosis. The necropsy specimens showed that the disease is not confined to the area that is thrombosed, and surgical resection of the entire diseased portion of the aorta could not have been accomplished.

Adequate lumbar sympathectomy will improve the peripheral circulation. This can be demonstrated by elevated oscillometric readings in some cases, normal skin temperatures, and relief of symptoms.

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RETROPERITONEAL HEMORRHAGE COMPLICATING PREGNANCY

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DURING the past 10 years retroperitoneal hemorrhage complicating pregnancy has been reported with increasing frequency. It has been described as a rare vascular accident, usually fatal to both mother and infant. Study of the literature, however, indicates that this complication (all types) should be considered uncommon rather than rare. It occurs often enough for the obstetrician to keep its possibilities in mind whenever pain, especially in the left side of the abdomen or pelvis, and evidences of intra-abdominal or pelvic hemorrhage have no other apparent cause. Because of the various sites whence bleeding may originate, retroperitoneal hemorrhage may simulate any of the hemorrhagic crises in the pregnant female, or the acute abdomen of any patient, pregnant or otherwise. Depending on the site of hemorrhage, period of gestation, and abruptness of onset, we may have to differentiate the following: ruptured peptic ulcer, ruptured spleen, biliary colic, renal colic, ectopic pregnancy, ruptured uterus, premature separation of the placenta, twisted ovarian cyst, and ruptured varicosities. The hemorrhage may occur before, during, or after childbirth. Forty-four cases of retroperitoneal hemorrhage complicating pregnancy have been found in the literature. We wish to present 4 additional cases, of which 3 were aneurysms of the splenic artery and 1 was an aneurysm of the renal artery, making a total of 48 cases.

CASE REPORTS

CASE 1. Mrs. P. S., a 35 year old white primi gravida, 1 week from term, with an uneventful prenatal course and a negative serology, complained of not feeling well and of vague upper abdominal discomfort. During the course of a telephone conversation with her family physician, she suddenly collapsed. On admission to St. Mary of Nazareth Hospital (1 hour later) the patient was dead. Relevant findings on autopsy were as follows: the abdominal wall was tense; sectioning of the peritoneum was followed by a gush of blood and clots. The uterus was full term in size, with no tears or lacerations. The fetus was stillborn with early maceration. The placental site was intact. The splenic and renal arteries were found intact with no evidence of aneurysm. The lesser omental sac contained about 500 cubic centimeters of blood and clots. Posterior to the lesser omental sac in the soft tissues of the retroperitoneum were large quantities of clots and blood, extending down the left iliac gutter and into the pelvis. Pancreas and kidneys failed to reveal evidence of hemorrhage. The spleen was not noteworthy. The anatomical diagnosis was: (1) full term pregnancy with intranatal death; (2) massive retroperitoneal hemorrhage with perforation into the peritoneal cavity, source undetermined, probably a branch of the splenic artery.

CASE 2. Mrs. H. W., a 23 year old white female, no prenatal care, entered the emergency room of St. Mary of Nazareth Hospital in poor condition and complaining of abdominal pain. She was a gravida 3, para 2 at term, with a rapid thready pulse, pallid complexion, rapid and shallow respirations, and a blood pressure of 60/0. The abdomen was large, tender to palpation, and no fetal heart tones were heard. There was a suggestive fluid wave. There was no evidence of vaginal bleeding. Rectal examination revealed a thick closed cervix. Clinical impression at this time was: (1) ruptured uterus, (2) ruptured varix in the broad ligament, (3) premature separation of the placenta. Blood and fluids were started immediately, and stimulants were given. As soon as the patient improved, surgery was done. The abdominal cavity was filled with fresh and old blood. Although the uterus was intact, the pregnancy was terminated by section, and stillborn male twins were delivered. The uterus was then packed to one side, the abdominal incision extended upward and to the left. Bleeding seemed to originate from the splenic artery near the splenic hilum. Because of the patient's poor condition, ligatures were applied through the mass of blood and clots about the splenic artery, and the site packed with gauze. No attempt at splenectomy was made. The patient received 500 cubic centimeters of plasma and approximately 1,200 cubic centimeters of blood during surgery. While the abdomen was being closed, the patient had a convulsive seizure. Her downhill course continued,

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and the patient died several hours later despite more blood and plasma.

Relevant findings on autopsy were as follows: the abdomen contained large quantities of blood and clots, estimated at 2½ liters. In the region of the splenic hilum there was a large quantity of clot. Direct section through this mass revealed an aneurysm about 4 centimeters in diameter arising from the splenic artery. The aneurysm has a thin wall and a bluish color to the lining. Anatomical diagnosis was: (1) massive retroperitoneal and intraperitoneal hemorrhage, due to a ruptured splenic aneurysm; (2) exsanguination. Microscopic diagnosis was: section of splenic artery aneurysm revealed a thinning of the wall in several areas with disappearance of the elastic lamella. In the same area, the media was shredded as if torn, with large amounts of fibrin and red blood cells attached to the surface of the vessel.

CASE 3. Mrs. L. C., a 32 year old colored primigravida, with an uneventful prenatal course, entered Provident Hospital in early labor with normal physical findings. Twelve hours later (12:00 noon), examination revealed a cephalic presentation, the cervix effaced and dilated to 5 centimeters, membranes intact, station at plus 1, fetal heart tones 148. One hour later (1:00 p.m.), the patient was found to be resting comfortably. One-half hour later (1:30 p.m.), the nurse noted that the patient was having difficulty in breathing. The resident physician was called at once and found her in shock. There was no perceptible pulse or blood pressure. Stimulants, plasma, and blood were started. At 1:40 p.m., the patient expired. An immediate postmortem cesarean section resulted in a full term stillborn fetus.

Autopsy revealed a ruptured aneurysm of the splenic artery, a massive intra-abdominal hemorrhage, extensive hemorrhage into the spleen and retroperitoneal tissues. At a level approximately 13 centimeters from the origin of the splenic artery was a large aneurysmal dilatation up to 4.5 centimeters in diameter. The distal portion of the sac was ruptured.

Microscopic diagnosis was: intima at many levels was thickened by hyalinized fibrous connective tissue. These changes extended, to a lesser degree, into the media. At some levels were many acicular slits where cholesterol had been dissolved.

CASE 4. Mrs. L. H., W/n, w/d, w/f of 24, primigravida, 7 months' gestation, entered St. Anthony of Padua Hospital, March 17, 1943, complaining of severe left abdominal pain, weakness, and faintness. These symptoms were of several hours' duration, and had had an abrupt onset. Positive physical findings were: pallid coloring, vomiting, pulse weak and rapid, blood pressure 60/0, uterus enlarged to about 30 weeks' gestation, fetal heart tones 146, some tenderness on uterine palpation but no rigidity, slight rigidity and some fullness over the left loin. There was no vaginal bleeding. Rectal examination revealed the cervix to be thick and closed. Preoperative impression was of abruptio placenta.

An intact, normal, pregnant uterus about 7 months' gestation was found, with hemorrhage in the left broad ligament, and free fluid in the peritoneum. A classical cesarean section was performed and the abdomen promptly closed.

Blood, sulfonamides, and fluids were given daily, but the patient failed to improve. The blood count fluctuated between 2.0 and 2.5, with the hemoglobin varying between 40 and 50 per cent. Nine days postoperatively a large tender mass, quite hard, extending from the iliac crest on the left side, to the costal margin, and from the midline to the left flank was evident. The patient expired on the tenth postoperative day.

Autopsy revealed that the left side of the abdomen was occupied by a large retroperitoneal mass which was about 30 by 20 by 13 centimeters. This mass involved the left kidney and adrenal, extending to and joining with the blood in the left broad ligament. The peritoneum over this mass was stretched and had a few scattered tiny tears where blood escaped into the abdomen. At a point just 2 centimeters from the origin of the left renal artery, on its anterior wall, was a 3 centimeter opening which led into a 13 centimeter outpouching. The anterior wall of this outpouching was completely missing.

Anatomical diagnosis was: (1) rupture of an aneurysm of the left renal artery; (2) hemorrhage within and about the left adrenal and into the left broad ligament; (3) perforated subacute duodenal ulcer sealed over by serosa over the gallbladder.

ETIOLOGICAL FACTORS

There is no one cause which is responsible for retroperitoneal hemorrhage, therefore, multiple factors must be considered. Among the contributing factors that have been mentioned in the literature are the following:

A. Pathologic entity (predisposing): (1) aneurysm; (2) periarteritis nodosa; (3) hemophilia; (4) nephritis; (5) tuberculosis of the kidney; (6) renal lipoma; (7) varicosity; (8) thrombosis, general angiitis of pre-eclampsia; (9) endocarditis and embolism; (10) essential hypertension; (11) hypervitaminosis (vitamin A) or avitaminosis (vitamin C).

B. Nonpathologic entity (precipitating): (1) trauma, e.g., blow, fall, kick; (2) coitus; (3) strain of bowel movement; (4) laughter; (5) coughing; (6) labor.

The possible role of hypervitaminosis (vitamin A) and avitaminosis (vitamin C) is very remote. Hemophilia, nephritis, and tuberculosis of the kidney have been stressed (by Halban and Seitz) because they are occasionally associated with perirenal capillary oozing.

These possibilities have not been verified in any of the cases studied. The role of hypertension and toxemia of pregnancy as causes of retroperitoneal hemorrhage has been discussed by Eastman: "there is no reason to believe that the relationship between pre-eclampsia and this accident is anything but accidental." Periarteritis nodosa may weaken the vessel and lead to the formation of single or multiple aneurysms; however, no such associated lesion has been described in the literature. Aneurysms, renal lipoma, endocarditis, and embolism have been proved. Trauma per se, e.g., kick, fall, blow, has not been listed in this series and, therefore, remains only a possibility. Coitus, straining with bowel movement, laughter, and excessive coughing have all been mentioned and contribute to the rupture of varix, vessel, or aneurysm by increasing the systemic blood pressure.

Most important of the contributing factors, we believe, are the changes in hemodynamics which occur during pregnancy and labor, with its added stress and strain. Weakened vessels subjected to the burden of increased circulatory volumes and increased systemic blood pressures of the pregnant female are more apt to rupture than those of the nonpregnant.

PERIOD OF GESTATION

The period of gestation is of no importance. Hemorrhage may take place at any time. The earliest incident occurred in a patient who was 2½ months pregnant (Potacki). This patient experienced pain in the abdomen immediately after coitus. The preoperative diagnosis was ruptured ectopic pregnancy or twisted ovarian cyst. Surgery revealed retroperitoneal hemorrhage in the region of the pancreas, left kidney, and probably the left renal artery. Most of the hemorrhages have been noted in patients who are in the third trimester of pregnancy. Four occurred in the puerperium (12 to 36 hours). Two occurred in active labor.

AGE

Most of the patients, regardless of cause, were between 25 and 35 years of age. The oldest patient was 45 years of age; the youngest, 18. It has been indicated that aneurysms as a rule, are found in individuals who are older than the great majority of expectant mothers (Danforth).

GRAVIDITY AND PARITY

These factors do not seem to be of any clinical significance. Hemorrhage has been noted in the primigravida as well as in the multigravida. Two patients, who were 39 and 45 years of age, are recorded as having been pregnant 12 and 11 times, respectively.

PATHOLOGY

Retroperitoneal bleeding may be from a vascular source (venous or arterial) or from a ruptured viscus. Hemorrhage, including our cases, has been reported from the following sites: (a) ruptured splenic aneurysm, 33 patients; (b) ruptured renal aneurysm, 7 patients; (c) ruptured uterine vein, 1 patient; (d) ruptured broad ligament varix, 2 patients; (e) ruptured varicosity of left ovarian artery, 1 patient; (f) ruptured aneurysm of hemorrhoidal vessel, 1 patient; (g) ruptured branch of celiac artery, 1 patient; (h) ruptured aneurysm of the external iliac artery, 1 patient; (i) ruptured renal lipoma, 1 patient.

The celiac artery (plexus) and its branches are apparently the most vulnerable of the medium sized distributing arteries, particularly the splenic artery which shows more natural predisposition to aneurysm formation than any other artery in the body. Many reviews of their incidence in the male and the nonpregnant female are recorded (Machener and Fuge; Baumgartner and Thomas). Every aneurysm is caused by congenital or acquired weakening of the arterial wall, usually due to a defect in the media. Those reported in this series have been predominately of the congenital type, with 1 instance of infective or mycotic type, and occasional arteriosclerotic type. The latter is characterized by atheromatous formations and calcification in the aneurysmal wall. The atheromatous lesion usually arises along the course of the main artery, while the mycotic lesion was found in a smaller branch of the artery. The congenital aneurysm is usually a singular sacular one which is found most frequently either at or near the branching points of the splenic artery.

Grossly, the aneurysmal wall is usually thickened, surrounded by old and fresh clots in which the fissure or rupture may or may not be discernible, depending on the size. Atheromas and calcifications, naturally, are more prevalent in the arteriosclerotic types. The rupture itself is variable in size, shape, and location, ranging from a small punched out area to an irregularly torn rip. Terms used to describe size have been cherry, hen's egg, goose egg, walnut, pea, apple, grape, hazelnut; others giving actual measurements, the largest being up to 9 centimeters.

Regardless of the type of the aneurysm, the outstanding microscopic finding is partial or nearly complete loss of elastic tissue in the media, with a partial or complete loss or reduplication of elastic tissue in the internal elastic lamina. The fibrosis so frequently described in these sections is undoubtedly a compensatory healing effort rather than a degenerative phenomenon.

Sheehan and Falkiner observed that during the course of pregnancy a number of patients have considerable splenic enlargement, usually associated with accidental hemorrhage or with anemia. They suggest that this enlargement is accompanied by some alteration of the blood supply to the spleen, and that this may be related to the high incidence of rupture of the splenic aneurysm recorded late in pregnancy.

The amount and extent of retroperitoneal hemorrhage depend on the size and location of the involved vessel or vessels. Rupture may occur in one or two stages. The initial hemorrhage occurs into the lesser sac, and massive hemorrhage into the peritoneal cavity may follow several days later. Splenic aneurysms may, in addition, rupture into the stomach, bowel, or body of the pancreas.

Renal vessel hemorrhage is associated with a hematoma of the flank (on the left side throughout this series) and may extend from the pelvis to the diaphragm, and from the aorta beyond the kidney. It may also extend into the left broad ligament, within the mesentery of the descending colon, and even to the lower border of the pancreas. Seven instances of ruptured renal aneurysms have thus far been reported.

SYMPTOMATOLOGY

Symptomatology varies with the size, location, and degree of damage in the involved vessel. Accordingly, the amount and extent of hemorrhage determine the patient's behavior. There is no constant picture. In order of frequency, symptomatology may be considered as follows:

Splenic Vessel Rupture. Symptoms of an unruptured aneurysm are variable or may be entirely lacking. Pain of a colicky nature in the epigastrium or hypochondrium may occur, and it is increased by exertion or changes of posture. There may be symptoms referable to the stomach, gallbladder, kidneys, or colon. A pulsating tumor may, on occasion, be felt. Recently, Sperling has re-emphasized Högler's triad of signs which may be of diagnostic value: (1) left upper quadrant pain, (2) a systolic bruit over a palpable tumor mass, and (3) a pulsating defect in the greater curvature of the stomach as shown by roentgenograms. If the initial hemorrhage is small and limited, the patient is most apt to present the following complaints: (1) pain—upper abdomen, epigastrium or hypogastrium, moderate to severe, possibly radiating to back, intermittent or persistent, most frequently on the left side; (2) abdominal tenderness—diffuse or localized, with or without distention; (3) fetal heart tones may or may not be present.

When the hemorrhage is massive, whether primarily or secondarily extending from the lesser sac, through the foramen of Winslow, into the general peritoneal cavity—the picture is more dramatic and critical: (1) patient is in shock or so impending; (2) pain in the upper abdomen which may be referred to the back or shoulder is not easily relieved; (3) abdominal tenderness is present with or without distention; (4) bowel sounds are depressed to absent; (5) repeated vomiting occurs; (6) urge for defecation is present; (7) melena or hematemesis is present if gastrointestinal tract is involved; (8) one or more convulsions occur; (9) uterus usually is in last trimester; (10) fetal heart tones cannot be made out; (11) patient may die immediately.

Renal Vessel Rupture. The following are indications that renal vessel rupture has occurred: (1) pain—usually in left loin, usually

of abrupt onset, intermittent or constant, moderate to severe; (2) abdominal tenderness as well as possible tenderness in left flank, with or without distention; (3) free peritoneal fluid; (4) mass in left flank; (5) rapid downhill course (7 patients reported have died).

Pelvic Vessel Rupture. Indications of rupture of splenic vessels consist of: (1) pain—lower quadrants, mild to severe, persistent; (2) mass—usually below or lateral to uterus, progressively larger; (3) uterus elevated or deviated to one side (usually right).

A discussion of bleeding from pelvic vessels may be divided into two parts: rupture of the external or internal iliac vessels, and rupture of the lesser branches of pelvic vessels. Rupture of the lesser branches of the pelvic vessels thus far reported occurred during or after delivery. The patients have been in good physical condition. The fetuses have not been affected by this type of hemorrhage which is in marked contrast to the fetal outcome of the hemorrhages associated with the splenic or renal vessels. All the mothers were already delivered of full term live fetuses. The pelvic mass may be palpable vaginally or outlined by roentgenograms. It may extend upward along the ureter to the kidney or diaphragm.

Aneurysms of the internal and external iliac vessels complicating pregnancy have also been reported. Of these, only one has been known to rupture during pregnancy.

PROGNOSIS

Retroperitoneal hemorrhage usually causes maternal and fetal death. This is particularly true if the hemorrhage is of splenic or renal origin. In the entire series of 48 patients, only 7 survived. Of even greater significance is the fact that only 2 out of 33 patients with splenic artery involvement lived through their ordeal. All 7 of the patients reported with ruptured renal aneurysms expired. The pelvic hemorrhages thus offer a more optimistic outlook. The patients who survived are listed as follows:

1. MacLeod and Maurice — ruptured splenic aneurysm, stillborn, 7 months' gestation.

2. Gilliam — ruptured splenic aneurysm, stillborn, 8 months' gestation.

3. O'Connor and Bradley—ruptured hemorrhoidal vein, live fetus, cesarean section, 8 months' gestation.

4. Scrivner—lipoma of left kidney, stillborn, 8 months' gestation.

5. Shull and Thoms—broad ligament hematoma, post partum, live fetus.

6. Kistner and Garber—ruptured broad ligament varix, stillborn, 7 months' gestation.

7. Priddle—ruptured aneurysm of external iliac artery, term pregnancy, live fetus, cesarean section.

TREATMENT

A correct preoperative diagnosis is seldom made. In some instances, the initial hemorrhage is small, though progressive. The patient when first seen may be in impending shock, or she may be dead. Assuming that blood transfusions and stimulants restore the patient to the status of fairly good operative risk, the preoperative diagnosis may be either an obstetrical hemorrhage or an acute abdomen. Surgical intervention eventually takes place. The surgeon invariably finds "a state of affairs that fill him with a sense of surgical plexity," particularly if the hemorrhage is of splenic or renal vessel origin (11). If it is a splenic aneurysm that has ruptured, the lesser omental sac and the peritoneal cavity may be full of blood, and fresh blood continues to ooze through the foramen of Winslow. If it is a renal vessel that has ruptured, there may or may not be free blood in the peritoneal cavity, but a large hematoma fills the flank, as previously described.

If the uterus is sufficiently large so as to interfere with adequate exploration, then a cesarean section or hysterectomy should be utilized as necessary. Since the fetus is invariably dead, its status need not be considered.

If there is gross blood in the peritoneal cavity, rupture of the uterus, rupture of an adnexal mass or vessel should be ruled out. After this is done and adequate exposure has been obtained, the upper abdomen must be fully explored. Unless the patient has a ruptured peptic ulcer or ruptured spleen, the bleeding is usually from the renal or celiac vessels. In order to follow the splenic vessel, the gastrocolic ligament must be resected and the lesser

sac exposed. The treatment of choice is a proximal ligature with removal of the aneurysm. The spleen will undergo aseptic atrophy.

If there is a large hematoma in the flank, the position of the renal pedicle should be ascertained, for a hemostat (or suture) may have to be applied on the pedicle nearest the aorta. Although the peritoneum over the hematoma has been incised, this procedure is not recommended, since the hemorrhage may be overwhelming. Ideally, the renal vessels are best approached through the flank. Since the abdomen is opened and the patient is in critical condition, it may be more expedient to extend the incision laterally and get more adequate exposure. Abdominal packing and tamponading are poor substitutes for adequately applied ligatures. Most patients who were packed with gauze over the bleeding site died anyway. One should attempt to ligate proximate to the rupture. Aberrant vessels should be particularly watched for. Whenever possible, these problems are best shared by the obstetrician with a general surgeon or a urologist.

Delay on the part of the patient in seeking medical aid or failure of the physician to comprehend the source and significance of the hemorrhage accounted for most of the deaths. This is particularly true in dealing with rupture of the splenic artery, its branches, or aneurysms. In at least 5 instances, several hours or more intervened between the initial attack and the onset of collapse. Naturally, there is little that one can do about the unfortunate patient who suffered a sudden massive hemorrhage and expired before or shortly after admission to the hospital.

Four cases of intact aneurysms of the internal iliac artery complicating pregnancy have been reported to date. The patient reported by Fothergill and Dougal was a 22 year old white female delivered of a full term fetus by cesarean section. During her postnatal examination a small pulsating mass the size of a tangerine was felt to the left of the uterus which was displaced to the right. The patient refused exploratory surgery. Eight months later she was admitted because the mass had continued to grow. At surgery she died of a massive hemorrhage. The aneurysm at this time was described as 3 times as large as on initial examination. Brunner reported on a patient who died suddenly 4 weeks after a spontaneous delivery, from the rupture of an aneurysm of the internal iliac artery. The aneurysm was not previously diagnosed. Brown and Soule have reported the presence of an aneurysm of the internal iliac artery, discovered during a cesarean section which was done because of a "pulsating mass which filled the entire right lower pelvis." One month later, the patient was operated upon by the surgical department and an endoaneurysmorrhaphy was performed. The patient died shortly after surgery, although no cause was mentioned.

MacLaren has shown that ligation of the internal or external iliac vessels during pregnancy can be done safely and should be performed as a lifesaving procedure wherever indicated. Priddle has recently indicated that ligation of the common iliac, if associated with paravertebral block and antispasmotics, does not necessarily result in gangrene of the extremity. When pelvic bleeding is profuse and uncontrollable, pressure on the aorta may be of invaluable assistance. Likewise, the aorta may and should be used for direct blood transfusions if the situation is critical. Prompt surgery and a little good fortune saved the lives of the patients reported by MacLaren and Priddle. The other 3 patients expired for reasons which have been indicated.

SUMMARY AND CONCLUSIONS

1. Four cases of retroperitoneal hemorrhage complicating pregnancy are herewith presented with a review of the literature.

2. Retroperitoneal hemorrhage complicating pregnancy is usually a fatal accident to both mother and fetus. In this series of 48 patients, only 7 survived. Two out of 33 patients with splenic artery involvement were reported as alive. All 7 of the patients with renal aneurysms expired.

3. This condition is more prevalent than the literature would indicate.

4. It may occur any time in pregnancy.

5. The bleeding may be vascular (arterial or venous) or visceral (ruptured viscus), and the sites as presented in the literature have been enumerated.

6. Initial hemorrhage may be small or massive, depending upon the type of rupture and the occurrence above or below the pelvic brim.

7. Symptomatology varies with the size, location, and extent of hemorrhage. There is no constant picture.

8. A correct preoperative diagnosis is seldom made, especially if the bleeding is above the pelvic brim.

9. The treatment of choice is the use of ligatures proximal to the perforation, with excision of any aneurysms and with splenectomy or nephrectomy, if indicated.

10. Retroperitoneal hemorrhage should be considered whenever pain, especially on the left side of the abdomen or pelvis, and evidence of hemorrhage have no readily apparent etiology.

11. Aneurysms, which are initially discovered during pregnancy or labor, should be treated as soon as possible. The longer treatment is delayed, the more apt we are to have a maternal death.

12. The external or internal iliac vessels may be ligated with safety. The ligation of the common iliac may result in gangrene of the extremity unless collateral circulation is established.

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THE BACTERIOLOGIC EXAMINATION OF TISSUE

THE development of chemotherapy for the treatment of infections during the past decade has made it necessary to know precisely the nature of the invading organism and, frequently, to determine its sensitivity to the various drugs available. The acute infections are generally recognizable clinically, and routine laboratory procedures usually suffice for isolating the organism. Chronic localized infections, however, often are not recognized clinically as such or they may present themselves in such a manner that bacteriologic examination of the lesion is not possible without surgical assistance. In these cases it has been a general policy among pathologists to make a histopathologic interpretation of the lesion and offer an opinion concerning the probable nature of the infection. In times past, such opinions were acceptable because in general each type of organism usually stimulates a tissue reaction somewhat characteristic for it. Until the appearance of satisfactory chemotherapeutic agents for infections, little harm was done by any inaccuracy in the histologic interpretation of a tissue reaction, because for most of the chronic localized infections, treatment was mainly symptomatic.

With surgical procedures becoming more extensively used for therapeutic and diagnostic purposes, and with routine roentgenologic examination of the thorax being widely employed to detect cancer and tuberculosis, it is important today to determine precisely the nature of the lesion that is found to be due to infection. This can be done with greatest certainty by bacteriologic examination of the tissue removed.

In a study of tissues removed for either therapy or biopsy accompanied by the histopathologic diagnosis of "tuberculosis," we were able to confirm such a diagnosis in only about 55 per cent of specimens by bacteriologic examination. This means that almost half of the patients concerned were spared the expense, inconvenience, and hazard of antituberculosis therapy.

On the other hand, careful bacteriologic study of tissues removed at operation has shown tuberculosis to be present when the histopathologic study of the tissue was interpreted as "nonspecific abscess," "Boeck's sarcoid," or "Hodgkin's disease." From the standpoint of the health of the individual as well as the general public, it is important to be able to recognize tuberculosis even when it masquerades as something else or is superimposed on another condition.

In our experience, as a general rule, tuberculosis is the most common single cause of chronic localized infections, whether they be

in lungs, lymph nodes, bone, skin, or elsewhere. Many other organisms, however, are known to produce lesions which simulate those of tuberculosis as they appear clinically, by roentgenologic examination or by histopathologic study. Many of the fungi will cause lesions simulating those of tuberculosis, and coccidioidomycosis can be a baffling imitator in this respect.

If the characteristic organisms are present in the lesion, the correct diagnosis may be established easily, but our experience has been that in lesions of long standing, it may not be possible to recognize them in the tissue sections, although culture will readily demonstrate their presence. We have had similar experiences with blastomycosis, histoplasmosis, sporotrichosis, and other fungous diseases. While we have no explanation for failure to find such organisms in the sections studied, we frequently find a great discrepancy between what is suspected (diagnosed) histologically and what is grown by bacteriologic procedures. In many such cases of coccidioidomycosis the result of the skin test is negative or the patient lives away from the endemic area, and only when the question is pressed will he admit having "visited" in the arid southwest, if only for a week.

Brucellosis is another disease which is likely to give rise to localized lesions of long duration, and many times they make their appearance several years after the initial acute onset. Such lesions may involve any of the bones, but especially those of the spinal column or extremities, bursa, kidneys, lymph nodes, prostate gland, epididymis, or fallopian tubes. Among some of these patients agglutination reactions will be negative for Brucella, thereby confusing the diagnosis unless the organism is isolated from the lesion. In a few instances we have been unable to isolate Brucella from localized lesions although the patients' Brucella agglutination reaction was positive. Such chronic lesions, due to Brucella, may appear histologically as a chronic nonspecific infection (often very mild in degree), or may very closely resemble the lesions of tuberculosis. Since many people have a positive reaction to a tuberculin skin test but have healed tuberculosis, it is very important to isolate the proper organism and to establish the correct diagnosis.

Infections caused by Salmonella (either as typhoid fever or as one of the less severe forms of salmonellosis) may give rise to local lesions which make their appearance some time after the acute onset. While typhoid fever is now considered a rarity in the United States, there is an occasional typhoid epidemic and salmonellosis, in general, is not uncommon. During World War II, there were many major epidemics of typhoid fever in the United States and Canada. With foreign travel becoming more extensive, it can be expected that an occasional localized infection caused by Salmonella typhosa will be encountered.

While the bacteriologic examination of tissue is desirable in order to isolate the etiologic agent, the surgeon carries considerable responsibility in making such studies successful. In many of the chronic lesions there may be very few organisms, and if only a drop of pus is collected on a swab and sent in for examination, the results may be fruitless. We have encountered several instances in which only a few colonies were present on the cultures, even though generous portions of the emulsion were used for the inoculum. It is thus evident that the material on a swab may be very inadequate, so far as the making of proper cultures for the common organisms is concerned, such as staphylococci, streptococci, typhoid organisms, Brucella, the various fungi, tubercle bacilli, and at times for Actinomyces, and so far as the search for Donovan

bodies, and the like, is concerned. To ensure a successful examination, it is necessary for the surgeon to select carefully the proper material and to send as much of it as is convenient to the bacteriology laboratory. For instance, it is recommended that a sinus tract be excised, together with the necrotic bone or lymph node from which it arises, since culture of material obtained from the cutaneous orifice of such a tract usually will show micrococci, Escherichia coli, or species of Pseudomonas which are common on the skin. When lymph nodes are removed, it is desirable to have a generous sampling, if more than one is available from a given area. Since, in a given group of nodes, not all may show the same condition, it is preferable to have one half of each of 4 nodes for either histology or bacteriology, rather than to have 2 of the 4 lymph nodes for each histopathologic and bacteriologic examination. Lesions from deep viscera (liver, lungs, spleen, kidneys) should be saved by putting a large portion in a sterile bottle in the operating room, the reason for this being that most pathology laboratories are not equipped to handle tissues aseptically. One very satisfactory procedure is to have on the instrument tray at the operating table a sterile wide-mouthed, screw-capped bottle of about 100 cubic centimeter capacity. In this can be put fluid, a large piece of tissue, thin pus from an abscess unexpectedly encountered or thick putty-like material from an inspissated abscess. If the lesion is proved to be a neoplasm, no harm will have been done. If it proves to be an infection, adequate material will have been held separate, suitable for bacteriologic study. If desirable or necessary, most specimens can be held in the refrigerator overnight until rapid histologic sections have been studied.

In addition to the surgeon's saving the proper material and in adequate amounts, he should supply the bacteriologist with the essentials of the history. To make a complete bacteriologic study of each and every surgical specimen is beyond the scope of even the most elaborate laboratory. But the history may suggest certain methods of study which otherwise would not be done. With the surgeon and the bacteriologist co-operating for the benefit of the patient, the chemotherapy of infections can be put on a fairly sound basis, but the indiscriminate use of such drugs is bound to be wasteful and at times dangerous, either to the patient or to the public with whom he comes in contact. LYLE A. WEED

"EMERGENCY" SPLENECTOMY?

THERE can be no question but that splenectomy must at times be performed as an emergency operation, notably in patients with injuries of the spleen or with spontaneous rupture. Aside from this indication, however, there seems to be a diminishing place for emergency splenectomy, even in such blood dyscrasias as acute fulminating thrombocytopenia of the "idiopathic" type and the hemolytic crisis. What with the constant development of newer diagnostic and therapeutic techniques, it has become possible to prepare patients for splenectomy more and more on an elective basis. Under such circumstances, an optimum degree of preparation rather than the severity of the patient's disease becomes the paramount consideration.

In hemolytic anemia of the acquired type and in the hemolytic crisis of the hereditary type there is a rapid destruction of the patient's own red blood cells which cannot usually be compensated for by blood transfusions. Transfusions, even of carefully matched blood, may be productive of severe reactions, thus aggravating an already serious situation. Extremely careful immunologic techniques

are often essential in such cases to delineate peculiar antibodies and to determine whether the reaction is one of the patient's serum against donor red cells or of donor plasma against patient's red cells. Coombs' tests, both direct and indirect, the use of bovine albumin as a diluent,[1] and the "provocative" plasma test[2] have all been used. In some of the patients with these conditions, reactions to a constituent in normal donor plasma occur and the "plasma" reaction[2] develops. In such cases, the use of washed red cells may be a lifesaving procedure. In the presence of a strong concentration of "cold" hemagglutinin, the administration of warm blood may make transfusions possible. Both the mortality and morbidity of splenectomy in the patients with severe hemolytic disease can be greatly reduced by careful preparation and attention to these immunologic details.

More recently, ACTH and cortisone have been used in acquired hemolytic anemia with striking results.[3,4] These hormones appear to have a direct inhibitory effect on the production of the autoantibodies which characterize the disease. As a result, the antibody becomes diminished and red cell destruction reduced. The effects have been dramatic in the great majority of the patients, so much so, that we did not perform a single splenectomy in 20 successive cases of acquired hemolytic anemia during a 2 year period. The excessive hemolytic activity is either stopped or controlled in the great majority of the cases, thus cutting down the need for transfusions almost entirely, and making splenectomy either unnecessary or a purely elective procedure in a "quiet" patient.

In idiopathic thrombocytopenia, the situation is not quite so clear-cut. We have recently discriminated sharply between acute and chronic forms of the disease.[5] Acute cases arise suddenly in previously well individuals and have a self-limited course. Although the situation may be extremely severe at onset, almost invariably there is a complete and permanent return to normality after a period of 2 to 12 weeks. Once the platelet counts have returned to normal values they remain persistently normal, despite their previously low values. Experience has shown that splenectomy done as an emergency procedure in these acute cases may not be wise. It is true that occasionally the results appear to be brilliant. However, not infrequently the platelet count either does not rise immediately or returns to normal later on. In other words, the regular "life span" of the disease may be unaltered, splenectomy or no splenectomy. It has thus become our rule to wait out an acute case, however trying this may be, meanwhile carrying out symptomatic therapy.

The situation is quite the reverse in the chronic cases in which the patient has had the disease, in its ups and downs, for years. The platelet count never reaches a normal level; bleeding from local sources such as the uterus, may be quite severe; and a hemorrhagic crisis may intervene at any time. Splenectomy in these cases is a necessity but is best done, as stated previously, during a remission.

The fact that all patients with idiopathic thrombocytopenic purpura, even of the chronic type, do not respond to splenectomy is another consideration which should reduce the

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enthusiasm for emergency surgical procedures in these cases. Thus the hemorrhagic crisis is best treated by medical measures, even though it must be conceded that there is a certain risk involved in this "wait and see" attitude. This risk, minimal in children, is certainly present in adults over forty in whom the possibility of cerebral hemorrhage must be kept ever in mind. The possibility of bleeding into the brain must be weighed against the very definite risk (24 to 30 per cent) of splenectomy during the acute crisis. The decision for or against splenectomy may be extraordinarily difficult, and each case must be judged on its merits. However, careful management, plus a good deal of patience, will often bring about a remission. This is usually followed by a complete cure in the acute, self-limited cases. Management includes the use of fresh whole, preferably siliconized blood, and the use of platelet rich blood from polycythemic donors.[5] ACTH and cortisone may also help to weather out a storm. Although the platelet count may not rise with these medications, the hemorrhagic tendency may become considerably diminished.

It must be conceded that the rationale and, indeed, the actual need of splenectomy in both the acute hemolytic crisis and the acute hemorrhagic crisis are at present in a period of reassessment. Except for splenic rupture, it appears that *emergency* splenectomy is a thing of the past. With careful medical handling, which includes the use of various therapeutic agents mixed with a pinch of judgment and a good deal of patience, one can convert these apparent emergencies to quiet and relatively undramatic situations. When this has been done, the decision for or against splenectomy can then be carefully and perhaps more intelligently appraised.

C. Stuart Welch
William Dameshek

THE SURGEON AT WORK

A SPLIT, SOLID, TUBE-LIKE CATHETER TO AID IN CUTTING THE SPHINCTER OF ODDI TRANSDUODENALLY

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IT IS not the purpose of this communication to discuss the indications for cutting the sphincter of Oddi, but to illustrate and to describe a small, solid tube-like device with its end split which greatly facilitates the cutting of the sphincter of Oddi when the duodenum and the common duct have been opened and a probe has been passed down through the sphincter into the duodenum so that the papilla can be located. By opening the common duct and passing a probe down to, or through, the sphincter of Oddi it has been possible for us to determine accurately at what point the duct enters the duodenum, and at what level it is desirable to make the longitudinal incision into the anterior wall of the duodenum in order to come directly on the papilla. Without a probe through the papilla, it has not been easy to locate accurately the level of the papilla. Nor has it been easy, when the anterior wall of the duodenum has been incised and the papilla demonstrated, to pass a probe upward into the minute opening of the duct into the duodenum or to keep this point—hidden as it so frequently is in the rugae of the duodenum—in sight and sufficiently quiet so that a probe can be readily passed up into it. Even with the common duct opened above and a probe or catheter passed down into it, we have often found it difficult to pass either the blade of a pair of scissors or a small knife blade up into the sphincter so that it can be accurately and cleanly cut for any desired length and under direct vision. It is our opinion that the method of incising the sphincter of Oddi under direct vision, with the duodenum opened, is superior to, and safer than, any plan of accomplishing this by passing an instrument down the duct with any form of knife blade to sever the sphincter without opening the duodenum.

In Figure 1a will be seen the solid, catheter-like tube which has been split for a distance of about 2 inches just proximal to its distal end. The common duct is opened just below the part where the cystic duct comes off, and a probe is passed down to the part where the common duct enters the posterior wall of the duodenum. The point of the probe is palpated through the anterior wall of the duodenum and a longitudinal incision is made through the duodenum at this point. The probe is passed through the sphincter at this point. This probe, which may be seen in Figure 2, has an eye drilled in its end. The solid rubber tube is cut obliquely so that it will easily pass back up through the sphincter, and a silk stitch is passed through its end and threaded through the eye of the probe. The solid, catheter-like tube can then be pulled back up into the duct and its end pulled out through the incision in the duct, or the tube may be passed down through the sphincter and into the duodenum. The tube is pulled into the duodenum until only the end that is split is resting in the duodenum just beyond the sphincter. Clamps then grasp both ends of the tube and a pair of right angle clamps are passed through the split in the tube which is located, as stated, just proximal to the end of the tube. However, sufficient tube is left to be caught by the clamp grasping the end of the tube. The jaws of the right angle clamps, which have been passed through the split in the end of the tube, are now separated to spread the tube, and the tube is pulled back into the duct until the spread end of the split tube, with one assistant pulling on the upper end and another pulling on the lower end, engages in the sphincter.

As can be seen in Figure 1b, with the split end of the tube spread and engaged in the sphincter, the right angle forceps can be opened to any distance until the sphincter is engaged and dilated to any desired distance, and one jaw of a pair of blunt pointed Metzenbaum scissors is passed through the dilated sphincter preparatory to sev-

From the Department of Surgery, The Lahey Clinic.

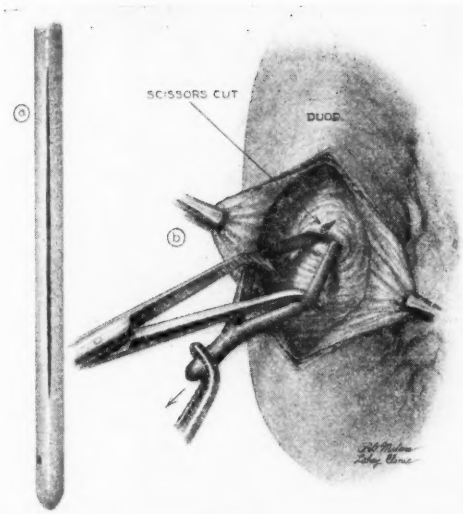

Fig. 1.

Fig. 1. In "a" may be seen a portion of the solid, split tube-like catheter which is approximately 1 foot long. Note that the end is perforated so that if it becomes necessary, a silk suture may be passed through it. Note the split in this solid, catheter-like round rubber tube. It is this split which when spread, as shown in "b," by right angle clamps puts the sphincter of Oddi so on the stretch that it can be severed at any height with a pair of scissors. Note in this illustration that a clamp is shown on the lower end of the split tube; the upper end of the tube which emerges through an incision in the common duct is not shown. By traction on the upper end of the tube emerging from an incision in the common duct and traction on the lower end, the tube is made taut so that when the split in its lower end is separated with right angle clamps, it can be drawn into the sphincter so that the sphincter is spread to any desired degree. This tube can be passed down the common duct, after it has been opened, through the sphincter and into the duodenum where it can be picked up, or a probe can be passed down the common duct into the duodenum and the upper end of the solid catheter-like tube can be withdrawn from below upward into the tube until the split portion, dilated with right-angle clamps, engages the sphincter.

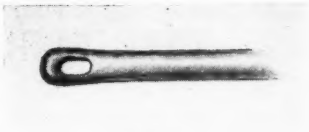

Fig. 2.

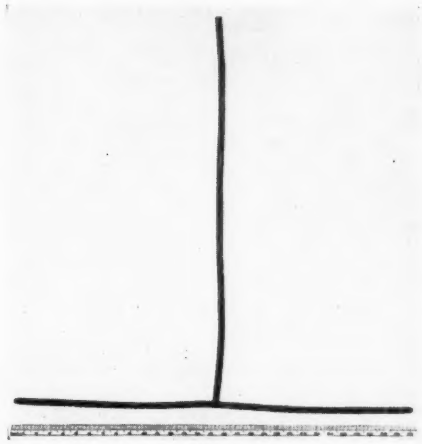

Fig. 3.

Fig. 2. Probe in which an eye has been drilled.

Fig. 3. Long limb T tube.

ering it. This makes it possible to sever the sphincter and duct to any desired distance and, under direct vision, to inspect the severed ends for possible bleeding. A suitable tube with a long limb, of the Cattell type (Fig. 3), is then introduced into the common duct, one end passing down into the duodenum, to be left in place for 3 to 4 months until suitable healing and molding of the severed sphincter has taken place. The longitudinal incision of the duodenum is then closed transversely first with an inverting layer of catgut and then with an interrupted layer of silk or cotton.

This has proved a simple, accurate method of making the sphincter of Oddi stand out so that it can be accurately cut with scissors and under direct vision.

It is important, with this split tube separated with the right angle clamps in the split, that traction be made upward and downward on the tube so that it is a firm structure which can be engaged in the end of the duct and separated, and that the split be held firmly engaged in the dilated sphincter. It is this firmly held split tube which fixes the dilated sphincter so that it can be severed with the scissor points engaged in it.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE important diagnostic problem of pain in the epigastric region is thoroughly analyzed in the fifth edition of Gutmann's book *Les syndromes douloureux de la région epigastrique*[1]. The first volume deals with the different causes of epigastric pain. In addition, the symptoms and methods of treatment of gastric and duodenal ulcers are presented. The author describes in an interesting chapter the periodicity in the occurrence of symptoms of ulcer, indicating that not only months but even years can separate two attacks of symptoms arising from an untreated ulcer. He, therefore, warns that one should be hesitant in attributing a cure to any therapeutic agent or program.

Cancer of the stomach is discussed extensively and critically. For many years Gutmann has pointed out that it is possible to make an early diagnosis of cancer of the stomach when the lesion is less than 1 centimeter in diameter and is still limited to the mucosa or has not yet invaded the muscularis mucosae. When a small lesion or niche, seen roentgenologically, is suspected, the author puts aside consideration of the diagnosis of ulcer until after he has carried out a therapeutic test for a month or two, during which time roentgenologic studies are made. An ulcer, he reasons, should heal; carcinoma will not. To be able to make an accurate diagnosis, complete understanding of all the clinical data is required, and much personal skill and experience are necessary. The subsequent chapters deal with diseases of the liver, gallbladder, and the bile ducts.

The second volume is concerned with perivisceritis, stenosis of the pylorus and duodenum, ptosis, gastritis, duodenitis, hemorrhage, malformations of stomach and diaphragm, and many other less common diseases. Dyspepsia is analyzed in a comprehensive chapter. The late postoperative complaints which follow operations on the stomach and gallbladder are considered in a section comprising more than 120 pages. To avoid much confusion, the reader should be aware that in France the term "peptic ulcer" means "postoperative ulcer," and it thus differs completely from the denotation of the term in this country.

It is somewhat surprising to find (vol. 1, p. 288) that the author administers vitamin A by rectum or intramuscularly, in view of the fact that these patients usually can take it easily by mouth. Furthermore, no mention is made of modern antibiotic agents in the matter of sterilization of the intestines.

A good improvement in this edition as compared with the 4 previous ones is the alphabetically arranged index. Unfortunately, some of the references are incomplete.

The author does not like statistics. It may be agreed that statistics sometimes are fallacious, but they none the less have a real value when scientifically compiled by a person especially trained in this field.

Gutmann says that North American authors seem to ignore publications written in French. Undoubtedly, the inability of many North American authors to read French is responsible for this situation. An English summary would, of course, be most helpful in this regard.

Since the author is an internist and not a surgeon, there is little technical information concerning the surgical approach to these problems. Gutmann should be congratulated for this excellent work. His publication contains an extensive number of reproductions of interesting roentgenograms. The volumes are well written, and should be of value to all who are interested in gastroenterology.

PAUL H. SEBRECHTS.

THE sixth section of the monumental work *Lehrbuch der Roentgendiagnostik*[2] is before us. The complete set of 10 sections, when published will constitute 5 volumes, as will also the English translation which is to follow as soon as possible. The first volume is on sale, the second volume in press, and the preparation of the third is well along toward completion.

This sixth section is devoted mostly to cardiovascular lesions, continuing the discussion of the chest begun in the fifth section. The highest standards of the printer's art are exemplified in this work. The illustrations are superb. The text is unusually interesting and very complete as to etiology, pathology, symptomatology, and roentgen diagnosis of the various cardiovascular lesions. The numerous illustrations are captioned in such detail that one derives much benefit simply from reading the illustrations. An attractive feature is the grouping of valuable tables of differential diagnosis. The experi-

[1] LES SYNDROMES DOULOUREUX DE LA RÉGION EPIGASTRIQUE. By René-A. Gutmann. Vols. 1 and 2, 5th ed. Paris: G. Doin & Cie, 1951.

[2] LEHRBUCH DER ROENTGENDIAGNOSTIK; No. 6, INNER ORGAN. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. 5th rev. enl. ed. Stuttgart: Georg Thieme; New York: Grune & Stratton, Inc., 1952.

ence of some of the world's greatest clinicians and the world literature have been drawn upon to supplement the work of the distinguished authors, most of them Swiss and Swedish but all of it is written in the German language. Section 7, in German, should appear before the end of June, with the other sections following. JAMES T. CASE.

THE publication *A Handbook of Operative Surgery: Surgical Gynecology; Including Important Obstetric Operations*[1] by J. P. Greenhill should prove to be a valuable reference for young gynecologists, general surgeons, and those in general practice who also perform operations. Although the book was written primarily with these men in mind, it should also make a worthwhile and interesting addition to the library of the more experienced gynecologist.

The technique of most gynecologic operations are depicted in step-by-step fashion. There are 101 well done, nicely reproduced pen and ink drawings. Each set of illustrations is accompanied by a concise, detailed, and clearly written description of the technique. The text not only emphasizes important surgical principles but also gives possible pitfalls and dangers which may be encountered in the procedure.

The author, the artist, and the publisher are to be commended for this excellent presentation.

JOHN W. HUFFMAN.

THE monograph *Surgery and the Endocrine System; Physiologic Response to Surgical Trauma—Operative Management of Endocrine Dysfunction*[2] consists of 143 pages and is divided into 2 major sections. The first section deals with the alarm reaction and the various mechanisms by which the patient survives injury. The relationship of the various endocrine glands in this complex mechanism is reviewed. The subjects of body fluid, shock, nutrition, convalescense, infection, and burns are discussed as to their dependence on the endocrine system.

The second section of the book of the monograph deals with endocrine therapy in surgical patients and the surgical treatment of the endocrine glands. An index is included.

This small volume will be found most useful to bring up to date those surgeons who have not kept pace with the newer developments in endocrinology. A good bibliography, appended to each chapter, will serve to provide further reading material to those interested. THOMAS C. DOUGLASS.

IN his fourth edition of *Office Endocrinology*[3], Robert B. Greenblatt has thoroughly rewritten and elaborated on the text of preceding editions. He presents the clinical aspects of endocrine problems which confront the practicing physician. The details of experimental groundwork, research theorems, and complicated hormonal assays of interest to the endocrinologist are not emphasized. Basic physiology is reviewed insofar as it will aid the physician when he is required to diagnose and test clinical endocrinopathies.

The author's style is refreshingly clear and concise. The material is presented in a manner almost outline in its directness. As a result each page contains a maximum of information. General endocrinology, diagnostic procedures, and male endocrinology are considered separately. Each section contains a brief and simple discussion of the character and treatment of the various endocrine disorders. Although individual exceptions may unquestionably be taken to some of the therapy the author advocates, it should be remembered that he is giving his experience in his own clinic and office. The book should appeal to, and be most useful to the general practitioners for whom it was designed. The sections on female endocrinology, hormonology, and diagnostic procedures should also interest the gynecologist and obstetrician. JOHN W. HUFFMAN.

IN a clear and concise manner, the authors of *The Metabolic Response to Surgery*[4] report on a series of complicated balance studies of nitrogen, potassium, and sodium on a group of normal volunteers, postoperative patients, and others who have been subject to trauma of various types. These studies are beautifully illustrated in a series of standard charts which render the complex data obtained easily understood by the reader. The separate effects of starvation, immobilization, and endocrine factors are clearly shown in examples. The depleted patient is studied and further reports are made of more complicated cases, such as those with large extrarenal losses, long convalescence, and burn patients.

The philosophy and rationale of attempts to change the metabolic balance is considered in a separate chapter.

The facts brought out by the studies (which have appeared in part in the current literature) are summed up in a separate chapter with specific advice as to clinical use of these facts. An appendix containing standard diets with accurate analysis of the various electrolytes is included. These are said to be accurate enough to serve as a guide for short balance studies without repetition of the food analysis.

This monograph is recommended reading for medical students as well as for doctors who have the privilege of helping guide patients through a convalescent period. Surgery owes a debt to authors of such publications as this, not only for the direct

[1] A HANDBOOK OF OPERATIVE SURGERY: SURGICAL GYNECOLOGY; INCLUDING IMPORTANT OBSTETRIC OPERATIONS. By J. P. Greenhill, M.D. Chicago: The Year Book Publishers, Inc., 1952.

[2] SURGERY AND THE ENDOCRINE SYSTEM; PHYSIOLOGIC RESPONSE TO SURGICAL TRAUMA—OPERATIVE MANAGEMENT OF ENDOCRINE DYSFUNCTION. By James D. Hardy, M.D., F.A.C.S. Philadelphia & London: W. B. Saunders Co., 1952.

[3] OFFICE ENDOCRINOLOGY. By Robert B. Greenblatt, B.A., M.D., C.M. 4th ed. Springfield, Ill.: Charles C Thomas, 1952.

[4] THE METABOLIC RESPONSE TO SURGERY. By Francis D. Moore, M.D., and Margaret R. Ball, A.B. Springfield, Ill.: Charles C Thomas, 1952.

contribution to our fund of knowledge, but to the stimulation of the imagination of other investigators.

THOMAS C. DOUGLASS.

THE monograph *Spleen Puncture*[1] translated from the German is of particular interest because it has been much less extensively used than has puncture of the marrow, glands, and liver. Hematological and differential diagnostic descriptions based on the study of over 300 spleen punctures are reported. With the technique described the procedure has been free of any danger. Only spleens that are enlarged are punctured and the test is never carried out in the presence of a hemorrhagic diathesis, acute septic spleen, or coma; it is performed only during full inspiration. Splenic puncture has proved a valuable clinical method of examination in the hematological and diagnostic sense, particularly if combined with a marrow puncture. Ample illustrations with tables, figures, color plates, and a bibliography add to the value of the book.

WALTER H. NADLER.

THE volume of 733 pages and 380 illustrations *Textbook of Surgical Treatment Including Operative Surgery*[2] is strictly confined to surgical treatment as indicated by the title. This includes preoperative and postoperative care, but does not include much in the way of etiology or discussion of signs and symptoms. Discussion of various methods of treatment of a given condition is very brief, and the results to be expected from the treatment described are not discussed at all. Operative procedures are described only in a general way.

Senior medical students will find this book useful as a reference, a place where the surgical management of most conditions can be found described in general terms. It will also be useful to junior residents in the same way.

DON ROBERTSON.

THE need for a textbook covering all phases of anesthesia practice has been great. In *Principles and Practice of Anesthesiology*[3] we have information which cannot be found in any other single volume.

This textbook comprises the essentials which are considered the minimum and necessary knowledge on the subject of anesthesiology. The information is concise, comprehensive, and documented from original sources. It is so arranged that it is easy for the reader to find any particular phase in which he may be specially interested. Minutiae previously unreported but widely practiced are set down in a most helpful manner. The basic physiology and pharmacology pertinent to anesthesiology are adequately described. Dr. Collins discusses complications and special procedures at considerable length. This section of the book is unique in that it is the only available digest of this material. Regional techniques are covered briefly.

The purpose of the publication has been to provide a comprehensive guide to the teaching and practice of clinical anesthesia. The author has surpassed his purpose and has succeeded in his endeavor. He has covered the field well.

The material is presented in a compact, attractive publication, on good paper, with sufficient illustrations and tables and with easily readable print. The excellent bibliography is arranged at the end of each chapter. The index is ample. Numerous typographical errors which appear will no doubt be corrected in later printings. Dr. Collins' style of writing is terse and telegraphic.

Practicing anesthesiologists, surgeons, and others will find this book a useful source of reference. It is a valuable textbook for undergraduates in medicine and for postgraduate students in anesthesiology.

MARY F. POE.

[1] SPLEEN PUNCTURE. By Privadozent Sven Moeschlin. Translated by A. Piney, M.D. New York: Grune & Stratton, 1951.

[2] TEXTBOOK OF SURGICAL TREATMENT INCLUDING OPERATIVE SURGERY; COMPILED BY 22 CONTRIBUTORS. 4th ed. Edited by C. F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S.E., F.R.F.P.S. (Glas.). Baltimore: The Williams & Wilkins Co., 1952.

[3] PRINCIPLES AND PRACTICE OF ANESTHESIOLOGY. By Vincent J. Collins, M.D. Philadelphia: Lea & Febiger, 1952.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

BATTLE CASUALTIES; INCIDENCE, MORTALITY, AND LOGISTIC CONSIDERATIONS. By Gilbert W. Beebe, Ph.D., and Michael E. DeBakey, M.D. Springfield, Ill.: Charles C Thomas, 1952.

RARE MANIFESTATIONS OF METABOLIC BONE DISEASE; THEIR PRACTICAL IMPORTANCE. 29th Annual Beaumont Lecture delivered before the Wayne County Medical Society, February 6, 1950. By I. Snapper, M.D., Ph.D. Springfield, Ill.: Charles C Thomas, 1952.

VETERANS ADMINISTRATION TECHNICAL BULLETINS, 1951; SERIES 10, VOL. 5. Washington: U. S. Government Printing Office, 1952.

TRANSACTIONS OF THE 11TH CONFERENCE ON THE CHEMOTHERAPY OF TUBERCULOSIS, JANUARY 1952. Edited by Veterans Administration, 1952.

BASIC MEDICAL PHYSIOLOGY. By W. B. Youmans, Ph.D., M.D. Chicago: Year Book Publishers, Inc., 1952.

EXPÉRIENCES SUR L'HÉMOSTASE BIOLOGIQUE EN NEUROCHIRURGIE ET INVESTIGATION DU PROBLÈME D'ANTIGENCITÉ DE LA THROMBINE. By Dr. Sisvan A. Gueukdjian. La Roche-sur-Yon, Switzerland: Imprimerie Centrale de l'Ouest, 1952.

LEHRBUCH DER GEBURTSHILFE. By Prof. Dr. Heinrich Martius, Prof. Dr. Werner Bickenbach, and Käthe Droysen. 2nd ed. Stuttgart: Georg Thieme, 1952.

TEXTBOOK OF GENERAL SURGERY. By Warren H. Cole, M.D., F.A.C.S., and Robert Elman, M.D., F.A.C.S. Foreword by Evarts A. Graham, M.D., F.A.C.S. 6th ed. New York: Appleton-Century-Crofts, Inc., 1952.